

**Biomechanical and Neurophysiological Changes  
Associated with Modified Head-lift and Effortful-  
Swallowing Rehabilitation Techniques**

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A Thesis Submitted in Partial Fulfilment of the  
Requirements for the Degree of  
Doctor of Philosophy

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Phoebe R. Macrae

Department of Communication Disorders

The University of Canterbury, Christchurch, New Zealand

29 August 2011



## Abstract

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Dysphagia can result from congenital disorders, structural damage, or neurological insult, therefore affecting individuals across the lifespan. Stroke is the leading cause of acquired dysphagia, with approximately half of stroke patients experiencing some level of swallowing impairment. Dysphagia negatively impacts survival and quality of life, highlighting a need for development of innovative and effective rehabilitative techniques. Management techniques have been developed to address disorders of swallowing but these techniques typically address symptoms of dysphagia rather than physiologic deficits. These techniques are often prescribed after neurological insult with little knowledge of their cumulative effect on swallowing biomechanics and neurophysiology. Effective treatment of dysphagia can only occur with knowledge of how commonly prescribed treatments influence all sensory and motor control aspects of swallowing. Without this detailed information, researchers are at risk of disregarding effective treatments, or employing treatments that are detrimental to unexamined swallowing processes.

There are many tools available for measuring change in swallowing biomechanics and neurophysiology. Many of these tools require further assessment of reliability, validity, precision, and responsiveness to assist researchers with selecting appropriate measures and adequately powering studies to detect treatment effects. A series of four methodological studies and a treatment study were undertaken as part of this research. The methodological studies aimed to contribute insights into aspects of reliability, validity, and precision assessment for the measures utilized in the treatment study. These elements together are crucial for formulating research studies aimed at providing empirical evidence for dysphagia treatment techniques.

The reliability of a novel method of calculating hyoid displacement with ultrasound relative to an anatomical reference point was investigated. This pilot study assessed intra- and inter-rater reliability across three raters for data analysis of five swallows from each of five healthy participants. The results suggest that the use of an anatomical reference point can alleviate the need for complex data calibration and transformation when utilizing ultrasound to quantify anterior hyoid displacement.

The utility of ultrasound to quantify the morphometry of the submental muscles was also assessed. Within-participant comparisons were made between coronal images taken with magnetic resonance imaging (MRI) and ultrasound in each of 11 healthy participants. These results suggest advantages of ultrasound over MRI, thereby endorsing the use of this less expensive and more accessible method.

Reliability and precision of longitudinal measures obtained with pharyngeal manometry were evaluated across three sessions in 20 healthy participants. This is the first study to have documented within-participant order effects and variance estimates for pharyngeal pressures. The results revealed no significant order effects but relatively large within-participant variance across sessions. These findings offer considerations for the use of manometry to document treatment outcomes, as considerable effect sizes, or substantial participant samples, are needed to supersede this variance.

Studies utilizing motor evoked potential (MEPs) to document effects of swallowing treatments rarely report details of data extraction or analysis. Therefore, an investigation was completed to compare various methods for quantifying MEPs from the submental muscles. This study used a pre-existing data set including five blocks of 15 MEPs from each of six healthy participants. Methods of analysis included quantification utilizing the mean of 15 individual trials, the median of 15 individual trials, the ensemble-average waveform, the ensemble-median waveform, and the rectified and averaged waveform. The most reliable onset latency measures across the five recording blocks were obtained when analysis was performed on the ensemble-median waveform. The most reliable amplitude/area values were obtained from the mean of the 15 trials and from the rectified and averaged waveform. Additionally, this study provided variance estimates across- and within-participants, providing a prompt for researchers and clinicians utilizing MEPs to consider this variance when determining desired effect sizes and sample sizes required to document evidence of treatment efficacy.

Part III of this thesis reports two treatment studies which independently assessed the cumulative effects (across six weeks) of effortful-swallowing and a modified head-lift manoeuvre on swallowing biomechanics and corticobulbar excitability utilizing the measures investigated in the methodological studies. Despite the common use of these two neuromuscular exercises in the management of dysphagia, discrepancies exist regarding the long-term effects of the head-lift manoeuvre on swallowing biomechanics, with no studies



addressing long-term modifications associated with effortful-swallowing. Furthermore, no studies have previously documented adaptations of corticobulbar excitability following either technique. The current study recruited 41 healthy older participants (mean age = 69 years, 20 males) who were alternately assigned to complete six weeks of either effortful-swallowing or modified head-lift exercise. Prior to initiation of the exercise protocol, baseline measures were taken using the following measurements: submental muscle MEPs induced by transcranial magnetic stimulation (TMS); oropharyngeal, hypopharyngeal, and upper esophageal sphincter (UES) pressures measured with pharyngeal manometry; submental muscle cross-sectional area (CSA) measured with ultrasonography; hyoid displacement quantified with ultrasonography; and submental muscle activation measured using surface electromyography (sEMG). For the effortful-swallowing group, the six-week exercise programme involved 33 effortful swallows, three times daily, five days a week. The number of repetitions was chosen to correspond to the head-lift manoeuvre protocol typically reported in the literature. The three daily sessions for the modified head-lift exercise involved 30 isokinetic head-lifts, and three head-lifts sustained for 30 seconds each. The isometric component was modified from the protocol recommended in previous literature, which proposes three sustained lifts for 60 seconds each. Participants completed the exercise at home and recorded their compliance on a weekly log sheet. Home visits occurred weekly to check the exercise execution and to monitor exercise maintenance. Within 2 days of concluding the exercise programme, participants returned for an outcome session consisting of the same measures as the baseline session. The results revealed no adaptations in swallowing biomechanics or corticobulbar excitability following six weeks of either exercise.

This research programme provokes consideration of the limitations of many measures used in swallowing research. Many of the measures used in swallowing studies have had very little research investigating their reliability, validity, precision, and responsiveness to treatment effects. Additionally, there is inadequate documentation of the magnitude of cumulative effects of rehabilitation techniques on swallowing biomechanics and neurophysiology. As these fundamental issues regarding measures utilized in swallowing research are addressed, researchers can be more confident in selecting appropriate measures, and adequately powering studies to detect treatment effects. This process will make treatment efficacy research less exploratory, and more reliant on logical consideration of the sensitivity of measures, and the magnitude of clinically relevant or desired treatment effects. This methodical approach to research is vital to justify the prescription of dysphagia rehabilitation

techniques with the aim of promoting long-term change in swallowing biomechanics and neurophysiology and, hence, functional swallowing.

## Acknowledgements

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Firstly, I wish to express my most sincere gratitude to my supervisors for their support and encouragement during the four years of my doctoral study. Their direction and unwavering confidence in my abilities resulted in an exceptionally efficient four years of research. Dr Maggie-Lee Huckabee's enthusiasm and curiosity in this area have inspired me to continue in a career of research with the same passion that she has shown. I greatly appreciate her mentoring and friendship.

Associate Professor Richard Jones has contributed unique input from a distinct field of expertise. Personally, I now aspire to reach the same level of organisational skills and attention to detail that Richard has modelled. I am fortunate to have received not only his professional and meticulous contribution to this research, but the balance he demonstrated with his enthusiasm for life outside of work.

Furthermore, I am very grateful to the participants of my research who each willingly gave six weeks of their time to enable me to complete this thesis. They not only opened their homes to me every week, but also showed a commendable tolerance of invasive procedures that I presented. In short, these participants enabled my research to be completed, and I am deeply appreciative of their generosity.

The many fellow students and colleagues at the Van der Veer Institute and the Department of Communication Disorders have contributed greatly to my development over the course of this research. They have provided me with valuable perspectives and considerations for my research, the light hearted conversation that helped to reduce the dullness of many days of writing, and of course the precious friendships that we've forged. A very special thanks to Sebastian Doeltgen for his solid support and continuing friendship, and warm appreciation to Sarah Wright, Petra Hoggarth, and Tracy Melzer who made my working space a supportive and happy environment. I also extend exceptional gratitude to Oshi Sella, whose contribution goes far beyond the pages of this thesis.

Richard Dove and Kathryn Greenfield from the Medical Physics and Bioengineering Department have been extremely committed in their technical support of this research, and Greg O'Beirne's patience and professionalism in his software ingenuity have been invaluable. I thank you all very much for making my research a reality. A large debt is owed to Daniel

Myall, who unwittingly got involved in a large proportion of this research. His advice and assistance with statistical analysis, publications, and thesis all happened alongside the crucial IT support that I so frequently called upon. His contribution to the revamp of this thesis was crucial, and I am extremely grateful for his ongoing willingness to explain and discuss. My gratitude also extends to John Pearson whose statistical advice was central to the resubmission of this thesis.

I would like to acknowledge the Neurological Foundation of New Zealand, the Todd Foundation, Health Research Council of New Zealand, and the University of Canterbury, all of whom have provided financial support throughout my doctorate. Special thanks also go to Kiri Manuera of the New Zealand Vice-Chancellors' Committee, who coordinated a lot of these awards and was a pleasure to deal with. I would like to extend my sincere gratitude to Douglas Ormrod of the Neurological Foundation, who has been a reliable point of call for all my funding enquiries, and who has offered me valuable advice on a career in research. I also extend my appreciation to Sonia-Ingrid Marshall of the post-graduate office, who offered prompt replies and personalized emails to help ease the many concerns regarding PhD policies.

Deepest thanks go to my mum, Denise, my dad, Dave, and my two brothers, Ben and Toby, who have supported me in their typical and warmly familiar style over the last four years. Their advice, opinions, and values still govern how I live my life, and for that I feel extremely lucky. And finally, to my partner Tim, who has sacrificed a lot in maintaining our relationship over the last two years, as well as keeping me healthy and well-fed! I look forward to what the next chapter holds.

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## Preface

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This PhD thesis conforms to the referencing style recommended by the American Psychological Association Publication Manual (5<sup>th</sup> ed.) and spelling recommended by Oxford Dictionary (<http://oxforddictionaries.com/>).

The research for this PhD thesis was carried out between October 2008 and October 2010 while the PhD candidate was enrolled in the Department of Communication Disorders, University of Canterbury. The research was based at the Van der Veer Institute for Parkinson's and Brain Research, and was supervised by Dr Maggie-Lee Huckabee and Associate Professor Richard Jones. The research was conducted during the tenure of a W. and B. Miller Doctoral Scholarship from the Neurological Foundation of New Zealand.

Aspects of this research were presented by the PhD candidate at the following conferences and meetings: The 17<sup>th</sup> Annual Meeting of the Dysphagia Research Society (New Orleans, Louisiana, March 2009), Biomouth Symposium (Dunedin, June 2009), Department of Communication Disorders Postgraduate Research Conference (Christchurch, November 2009), The 18<sup>th</sup> Annual Meeting of the Dysphagia Research Society (San Diego, California, March 2010) – awarded 2<sup>nd</sup> Place Scientific Abstract (poster presentation), University of Canterbury College of Science 'PhD in 3' final (Christchurch, May 2010), and Biomouth Symposium (Christchurch, June 2010).

The following publications were generated during this PhD research (three additional papers are under review):

### ***Full papers***

Huckabee, M-L., & **Macrae, P.** (2009). Temporal resolution in swallowing neural control: The way forward (Editorial). *Clinical Neurophysiology*. 120(10), 1764-1765.

Al-Toubi, A., Abu-Hijleh, A., Huckabee, M-L., **Macrae, P.**, & Doeltgen, S. (2010). Effects of repeated volitional swallowing on the excitability of submental corticobulbar motor pathways. *Dysphagia*. (Online, DOI: 10.1007/s00455-010-9313-1).

**Macrae, P.,** Myall, D., Jones, R., & Huckabee, M-L. (2011). Pharyngeal pressures during swallowing within and across three sessions: within-subject variance and order effects. *Dysphagia*. (Online, DOI: 10.1007/s00455-010-9324-y).

Doeltgen, S., **Macrae, P.,** & Huckabee, M-L. (2011). Pharyngeal pressure generation during tongue-hold swallows across age. *American Journal of Speech Language Pathology*. 20, 124-130.

**Macrae, P.,** Doeltgen, S., Jones, R., & Huckabee, M-L. (2012). Intra- and inter-rater reliability for analysis of hyoid displacement captured by ultrasound. *Journal of Clinical Ultrasound*. 40(2), 74-78. (Online, DOI: DOI: 10.1002/jcu.20874)

### ***Book chapters***

Huckabee, ML., **Macrae, P.** (accepted, in press): Management and Treatment of Oropharyngeal Dysphagia – Adult: Rehabilitative Maneuvers and Exercise: Effortful Swallow. In: Manual of Diagnostic and Therapeutic Techniques for Disorders of Deglutition. Shaker, R., Postma, G., Belafsky, P., Easterling, C. San Diego: Springer.

### ***Refereed conference abstracts***

**Macrae, P.,** Huckabee, M.-L., Doeltgen, S., & Jones, R. (2009). Intra- and inter-rater reliability of hyoid displacement measured by ultrasound. *Dysphagia*, 24(4), 482-483.

## List of abbreviations

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1D	one-dimensional
2D	two-dimensional
3D	three-dimensional
ANOVA	analysis of variance
C1	cervical spinal nerve 1
C2	cervical spinal nerve 2
CI	confidence interval
CN	cranial nerve
CN V	cranial nerve 5
CN VII	cranial nerve 7
CN IX	cranial nerve 9
CN X	cranial nerve 10
CN XII	cranial nerve 12
CPG	central pattern generator
C <sub>z</sub>	cranial vertex
DSG	dorsal swallowing group
EEG	electroencephalography
EMG	electromyography
ERP	event related potential
FEES	fibreoptic endoscopic evaluation of swallowing study
fMRI	functional magnetic resonance imaging
GERD	gastroesophageal reflux disease
ICC	intra-class correlation coefficient
M1	motor strip, Brodmann's area 4
MEG	magnetoencephalography
MEP	motor evoked potential
MRI	magnetic resonance imaging
NA	nucleus ambiguus
NMES	neuromuscular electrical stimulation
NTA	nucleus tractus solitarius
OTT	oral transit time

PET	positron emission tomography
PPI	proton pump inhibitor
PTT	pharyngeal transit time
RLN	recurrent laryngeal nerve
rTMS	repetitive transcranial magnetic stimulation
S1	sensory strip, Brodmann's area 3
SD	standard deviation
sEMG	surface electromyography
SLN	superior laryngeal nerve
SMA	supplementary motor area
SPECT	single photon emission computed tomography
SRT	swallowing response time
tDCS	transcranial direct current stimulation
TTL	transistor-transistor logic
UES	upper esophageal sphincter
VFSS	videofluoroscopic swallowing study
VSG	ventral swallowing group



## **PART I: INTRODUCTION**



# Chapter 1: Introduction

---

Dysphagia is associated with increased length of hospital stay, disability, death, and institutional care. The consequential effects of aspiration pneumonia, malnutrition, dehydration, and reduced quality of life complicate recovery in a substantial proportion of patients. Not only do such complications pose a substantial cost to healthcare systems but they reduce the likelihood of successful recovery in such patients. With as many as 80% of stroke patients predicted to experience impaired swallowing, there is an urgent need to develop effective treatments to reduce the burden of dysphagia on patients and healthcare providers.

This project addressed two distinct but related aspects of swallowing research: methods of measuring biomechanical and neurophysiological adaptations in swallowing, and the effect of rehabilitation techniques on these measures. Part I of this thesis provides an introduction to normal and disordered swallowing, an essential foundation for any investigation into swallowing rehabilitation. Part II presents four methodological investigations. These studies were largely developed to augment the research reported in Part III but offer distinct points for discussion given their methodological focus. Part III presents a treatment study which investigated the effects of two commonly prescribed rehabilitation techniques on swallowing biomechanics and corticobulbar excitability of healthy participants: effortful-swallowing and the head-lift manoeuvre. Part IV provides concluding remarks considering the research presented in all the preceding sections.

Methodological studies are considered a crucial component in the investigation of dysphagia rehabilitation procedures. As raised in the various discussions throughout this thesis, there is considerable work to be done to improve the certainty of results and conclusions in swallowing rehabilitation studies to date. Swallowing research is a relatively new area of focus, and foundation research is still required to ensure the basic components of the measurement tools used are complete. Because of the vast array of measures and patient populations available, fulfilling this requirement is an immense undertaking. Each area of swallowing research needs to address the concerns specific to its measures and population to reduce the limitations of current methods.

The methodological investigations presented in Part II aimed to enhance the application and interpretation of the measures used in the treatment study by addressing components of reliability, validity, and precision assessments of the measures. Ideally such methodological clarifications would have preceded the treatment study but reservations regarding the precision, and therefore sensitivity of these measures to treatment effects – previously utilized in swallowing research – emerged during the course of data collection for the treatment study. Therefore, the majority of the two aspects of the research programme were conducted in parallel. Implications from the methodological studies have been incorporated into data collection and analysis of the treatment study. However, additional suggestions for future studies are also provided based on the fact that not all uncertainty regarding the responsiveness of these measures could be clarified. One of the issues considered in the Discussion of Part II is the need for reliability, validity, and precision assessments of measures to incorporate the target population. As there are many measures available in swallowing research, investigation of all of these was beyond the scope of this research. Therefore, the methodological studies were used to further enhance the use of the measures specific to the treatment study.

Chapter 3 provides a detailed review of the literature for measuring change in a select number of swallowing parameters. Chapter 4 outlines objectives derived from this literature to be addressed in the methodological studies. Chapter 5 investigates a novel method of assessing hyoid displacement with ultrasound. This study improved on methods previously reported, eliminating the need for complex data calibration and transformation. Chapter 6 describes a study aimed at validating ultrasound for measuring the size of the swallowing musculature. This study identified advantages of ultrasound over the ‘gold standard’ measure of magnetic resonance imaging (MRI) for the submental muscles and, hence, enhances methods of muscle quantification. Chapter 7 compares data extraction methods for quantifying measures of corticomotor function. This study provides considerations for analysis of motor evoked potentials (MEPs) induced by transcranial magnetic stimulation (TMS) to document corticobulbar excitability associated with swallowing. This chapter also quantifies the variance seen in healthy participants across sessions in the absence of treatment, giving insight into the precision of MEPs as a measure. Chapter 8 describes a study undertaken to determine the reliability and precision of pharyngeal pressure measures. This study provided results that are integral to the emergence of manometry as a viable measure by specifying

precision estimates against which future studies can determine appropriate effect sizes and sample sizes. Chapter 9 integrates and discusses the findings of the methodological studies and the existing limitations of these measures.

Part III presents a major study undertaken to investigate changes associated with effortful-swallowing and a modified head-lift manoeuvre. While rehabilitation based upon these techniques is increasingly recommended, the evidence to support the prescription of these techniques is minimal. Studies have typically documented immediate effects of treatment techniques on various swallowing parameters, with very few having addressed cumulative effects. Therefore, the rehabilitative potential and efficacy of many swallowing treatments remains unknown. To enhance clinical competence in dysphagia management, and to justify rehabilitation protocols for patients, the effectiveness of the techniques needs to be demonstrated.

Chapter 10 provides a review of the literature relevant to the rehabilitation of dysphagia with effortful-swallowing and head-lift manoeuvre. Chapter 11 proposes hypotheses based on this review. Chapter 12 details the methods and Chapter 13 reports the results. Chapter 14 provides a discussion covering the possibilities for the results documented in the treatment study.

While the sections of this thesis are related, they have been segregated to aid in discussion pertinent to methodological factors as distinct and substantial issues from the treatment study. The interaction of these two concepts is discussed in the concluding chapter, Part IV.



## Chapter 2: Literature review – Normal and disordered swallowing

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### 2.1 Biomechanics of swallowing

Swallowing is one of the most complex neuromuscular tasks executed by humans, requiring precise coordination of between 34 (Daniels & Huckabee, 2008, p. 119) and 38 (Perlman & Christensen, 1997) pairs of muscles in just over one second (Kendall, McKenzie, Leonard, Goncalves, & Walker, 2000). Models of swallowing biomechanics typically divide the process into three or four phases (Perlman & Christensen, 1997). All frameworks include the oral phase (which incorporates oral preparatory and oral transport/transit), pharyngeal phase and the esophageal phase (Perlman & Christensen, 1997), with four-phase models incorporating either a pre-oral phase (Daniels & Huckabee, 2008), or differentiating the functions of bolus preparation and transit as separate phases (Logemann, 1983). These phases are physiologically interconnected, but distinguishing between them helps best explain the biomechanical and neural control mechanisms associated with the swallowing process as a whole. The discussions in this chapter will utilize a four-phase model of swallowing: pre-oral, oral (incorporating both preparation and transit), pharyngeal, and esophageal phase (Daniels & Huckabee, 2008). Although discussed as separate processes, the interdependence of the phases must be considered throughout (Figure 2.1).

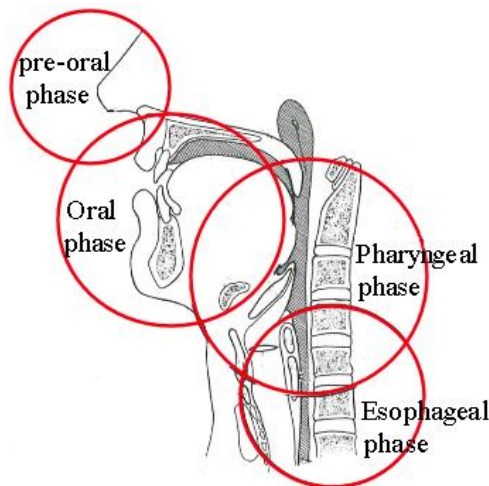


Figure 2.1<sup>1</sup>. Interdependence of the four phases of swallowing.

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<sup>1</sup> Adapted from Bass, Bass, N., & Morrell, R. (1992). The Neurology of Swallowing. In M. Groher (Ed.), *Dysphagia: Diagnosis and Management* (Second ed.). Massachusetts: Butterworth-Heinemann.

Swallowing has been described as a “single pressure-driven event” (Perlman & Christensen, 1997, p. 18), with the oral and pharyngeal cavities forming a continuous chamber. Four valves modulate the pressure within the chamber (Figure 2.2); the lips, velopharyngeal port, larynx, and the upper esophageal sphincter (Perlman & Christensen, 1997). This model of swallowing biomechanics highlights how the integrity of one phase is reliant on the integrity of the others.

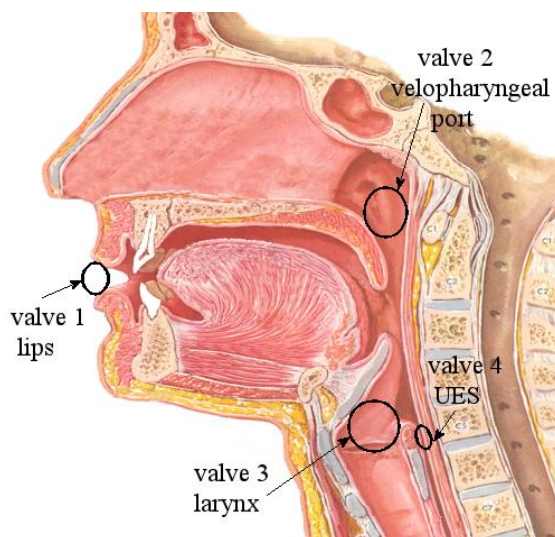


Figure 2.2<sup>2</sup>. Schematic of the four valves that modulate the pressure within the oral and pharyngeal chamber.

### 2.1.1 Pre-oral phase

The pre-oral phase emphasizes the influence of non-specific swallowing behaviours such as sight, smell, attention, and cognitive function on the ensuing swallowing biomechanics. The inclusion of the pre-oral phase acknowledges the importance of cognitive functions in swallowing, historically considered beyond the realm of cerebral control. This phase involves recognition and cortical processing of visual and olfactory characteristics of the bolus to be ingested (Daniels & Huckabee, 2008). Such processes influence salivary production and, dependent on bolus characteristics, early airway protection (Daniels & Huckabee, 2008).

### 2.1.2 Oral phase

The oral phase represents the aspects of swallowing that are under voluntary control (Donner, Bosma, & Robertson, 1985; Ertekin & Aydogdu, 2003). It involves acceptance,

<sup>2</sup> Adapted from Netter, F. H. (1971). *Digestive system. Part I: Upper digestive tract* (The Ciba Collection of Medical Illustrations. Vol. 3). New York: Ciba.



preparation/manipulation, and transport of the bolus into the pharynx (Perlman & Christensen, 1997). The lips are responsible for removing textures from surfaces such as utensils or cups and sealing the anterior aspect of the oral cavity (Miller, 1999). The anterior seal formed by the lips also contributes to a build-up of pressure in the pharynx by providing the first of the four valves in the pressure system required for effective bolus transfer (Perlman & Christensen, 1997). The tongue tip grooves to form a basin in which the bolus is positioned when it enters the oral cavity (Perlman & Christensen, 1997). The tongue base contacts the soft palate to seal off the oral cavity from the pharynx, protecting the open airway until bolus preparation is complete (Daniels & Huckabee, 2008; Miller, 1982; Perlman & Christensen, 1997). This contact between the base of the tongue and the soft palate is known as glossopalatal seal ('glossus' meaning tongue). Figure 2.3 shows the position of anatomical landmarks involved in swallowing.

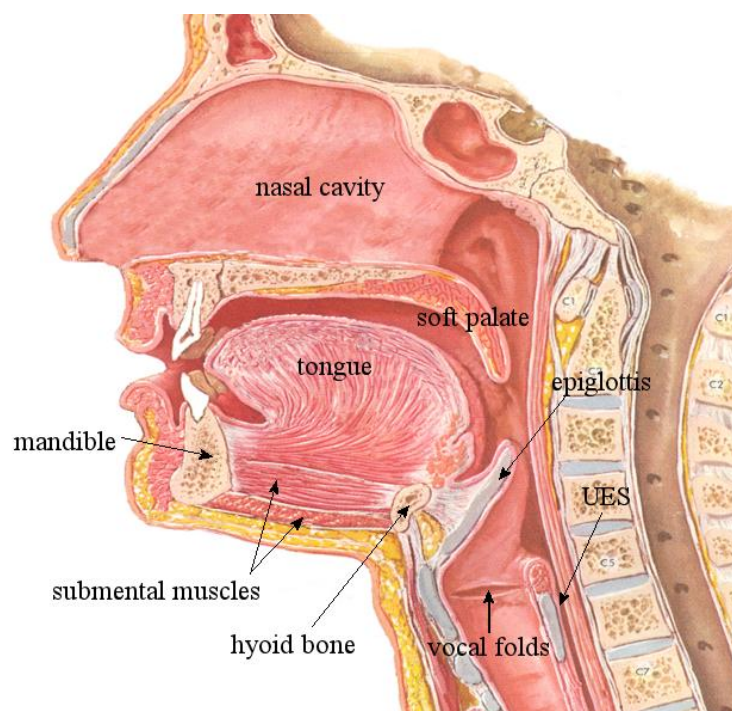


Figure 2.3<sup>3</sup>. Sagittal cross-sectional of the head and neck.

Preparation of liquid boluses prior to transfer into the pharynx may be minimal, with the muscles involved in opening (anterior belly of digastric, mylohyoid and geniohyoid) and closing (masseter, temporalis, medial pterygoid) the jaw recruited for mastication of heavier textures (Bass & Morrell, 1992). Maintaining such textures within the surface of the teeth during mastication is achieved outside of the teeth by activation of the buccinator muscles

<sup>3</sup> Ibid.

(Bass & Morrell, 1992; Perlman & Christensen, 1997) and from inside of the teeth by midline rise of the tongue (Daniels & Huckabee, 2008). The buccinator muscles line the cheeks and contract to flatten them against the teeth (Perlman & Christensen, 1997). The lateral and protrusive movement of the jaw required to grind food is accomplished with alternate activation of the lateral pterygoid muscles that sit either side of the jaw (Bass & Morrell, 1992). Bolus preparation is largely voluntary, so duration of this part of the oral phase is highly variable according to bolus properties and individual inclination.

Prior to transfer of the bolus into the pharynx, the vocal cords approximate (Zamir, Ren, Hogan, & Shaker, 1996) along with cessation of respiration to protect the lungs from the descending bolus (Martin-Harris, Brodsky, Price, Michel, & Walters, 2003). Swallowing usually takes place mid-expiration in the respiratory cycle (Kelly, Huckabee, Jones, & Frampton, 2006; Martin-Harris et al., 2005), presumably so that any texture that enters the laryngeal inlet during swallowing is expelled with completion of expiration (Kelly, et al., 2006; Martin-Harris, et al., 2005). To transport the bolus from the oral cavity into the pharynx, the glossopalatal seal is relaxed and the tongue base is pulled down by the hyoglossus and genioglossus muscles (Perlman & Christensen, 1997). Contact between the tongue and the hard palate starts at the tip of the tongue and moves sequentially backwards to squeeze the bolus towards the pharynx (Perlman & Christensen, 1997). Transfer of the bolus typically takes less than 1 s (Daniels & Huckabee, 2008). The oral phase of swallowing ends with the onset of the pharyngeal phase of swallowing.

### **2.1.3 Pharyngeal phase**

The pharyngeal phase of swallowing involves numerous biomechanical events in rapid succession, completed in less than 1 s (Kahrilas, Lin, Chen, & Logemann, 1996; Kendall, et al., 2000). Historically, the pharyngeal swallowing response was considered to be out of the realm of voluntary control (Dodds, 1989; Donner, et al., 1985), but more recent evidence suggests that components of this phase may be modulated through volition (Jafari, Prince, Kim, & Paydarfar, 2003; Ohmae, Logemann, Kaiser, Hanson, & Kahrilas, 1996). The initiation of the pharyngeal phase begins with rapid onset of muscle activation in a number of muscles, referred to as the “leading complex” (Doty & Bosma, 1956). Investigations have shown the components of the leading complex and the successive activation of other muscles involved in the phase to be highly reproducible (Doty & Bosma, 1956), lending to the idea of

a central control mechanism for this phase (Perlman, Palmer, McCulloch, & Vandaele, 1999). However, swallows recorded during more natural deglutitive situations show considerable variability in the order of activation for individual muscles across individuals (Gay, Rendell, & Spiro, 1994a; Gay, Rendell, Spiro, Mosier, & Lurie, 1994b; Spiro, Rendell, & Gay, 1994), suggesting some adaptation to the ‘reflex’ pattern from higher level neural influences (Gay, et al., 1994a; Robbins et al., 2008). Key events occurring in the pharyngeal phase are detailed below.

**Hyolaryngeal excursion:** Hyolaryngeal excursion is the biomechanical event responsible for lifting the larynx and hyoid bone in both an anterior and superior direction (Perlman & Christensen, 1997). Superior excursion is achieved through contraction of the hyoglossus and mylohyoid muscles (Miller, 1999), with facilitation from the stylohyoid and posterior belly of digastric muscles (Daniels & Huckabee, 2008). Anterior excursion is achieved through contraction of the submental muscles (Goyal, 1984), consisting of the anterior belly of the digastric, mylohyoid, and geniohyoid muscles. The paired anterior belly of digastric is the most superficial muscle of the three pairs (Figure 2.4a), with attachments at the hyoid bone and the inner side of the lower border of the mandible, slightly lateral to the symphysis (Gray, 1977). The paired mylohyoid muscles (Figure 2.4b) form the floor of the oral cavity with its flat triangular shape that attaches around the internal margin of the mandible (Perkins & Kent, 1986). The muscles are joined down the midline by a fibrous median raphe that extends from the mental symphysis to the hyoid bone (Gray, 1977). The deepest of the three submental muscles are the paired geniohyoid muscles (Figure 2.4c). These muscles sit at midline with attachments at the mental symphysis and the hyoid bone (Perkins & Kent, 1986). The mandible is fixed at the initiation of the pharyngeal swallow (Hila, Castell, & Castell, 2001), therefore contraction of these muscles results in superior and anterior displacement of the hyoid bone. Similar displacement is also evident for the larynx due to the muscular connections between the hyoid and the larynx (thyrohyoid muscles).

Contraction of the submental muscles for hyolaryngeal excursion is a primary component of the “leading complex” (Crary, Carnaby Mann, & Groher, 2006; Doty & Bosma, 1956), highlighting the importance of this event for the initiation and efficacy of the pharyngeal swallow. Contraction of the submental muscles influences other biomechanical events crucial to passageway of the bolus through the pharynx into the esophagus. The results of

hyolaryngeal excursion are two-fold: The epiglottis is biomechanically tilted (Vandaele, Perlman, & Cassell, 1995) to assist airway protection, and the upper esophageal sphincter (UES; zone separating the pharynx from the esophagus) is pulled open (Perlman & Christensen, 1997) to allow bolus transfer from the pharynx to the esophagus. The biomechanical events reliant on hyolaryngeal excursion make the submental muscles a common target for many swallowing therapy techniques (Doeltgen, Dalrymple-Alford, Ridding, & Huckabee, 2010a; Shaker et al., 1997; Suiter, Leder, & Ruark, 2006).

Velopharyngeal closure: Closure of the velopharyngeal port prevents the bolus from entering the nasal cavity, and is achieved through activation of the palatopharyngeus and levator veli palatine muscles of the soft palate to seal the nasopharyngeal port (Miller, 1999). It is the 2<sup>nd</sup> of the four valves in the swallowing pressure system, contributing to the build up of pressure in the pharynx necessary for effective bolus clearance (Perlman & Christensen, 1997).

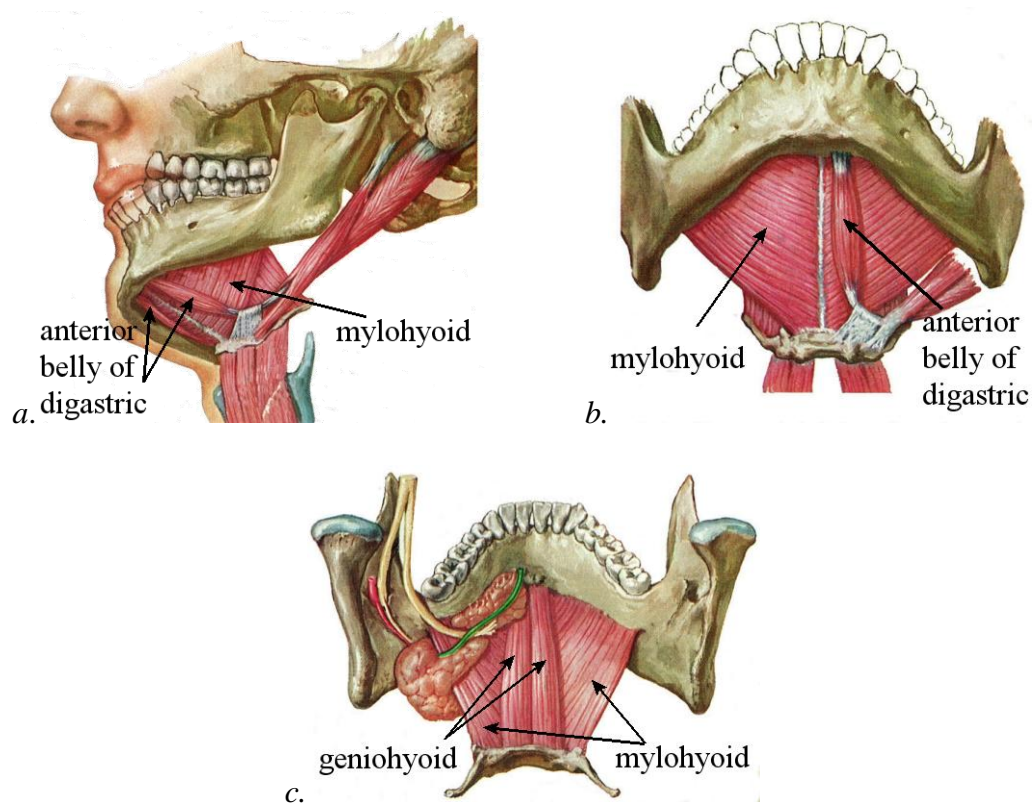


Figure 2.4<sup>4</sup>. The submental muscles: anterior belly of digastric (a), mylohyoid, (b) and geniohyoid (c).

<sup>4</sup> Ibid.

**Laryngeal closure:** A multifaceted arrangement protects the airway as the bolus passes by the laryngeal inlet towards the esophagus (Daniels & Huckabee, 2008). Further to approximation of the vocal cords in the oral phase, the vocal folds and false vocal folds adduct completely (Daniels & Huckabee, 2008), and the arytenoid cartilages approximate the epiglottis (Perkins & Kent, 1986). The deflected epiglottis resulting from hyolaryngeal excursion adds the uppermost layer to this complex airway protection system (Perlman & Christensen, 1997). These mechanisms together compress the mucosal lining of the laryngeal vestibule (quadrangular membrane), which ‘plugs’ the airway for further protection (Daniels & Huckabee, 2008). As well as protecting the lungs from the bolus, laryngeal closure contributes to the build-up of pharyngeal pressure during swallowing by providing the 3<sup>rd</sup> valve of the swallowing pressure system (Perlman & Christensen, 1997).

**Base of tongue to posterior pharyngeal wall approximation:** The squeeze of the tongue on the bolus in the oral phase is continued in the pharyngeal phase by the retraction of the base of the tongue towards the posterior pharyngeal wall (McConnel, Cerenko, & Mendelsohn, 1988). This provides direct pressure on the descending bolus, and also facilitates pressure build up in the pharynx.

**Pharyngeal contraction:** The pharyngeal constrictor muscles form the walls of the pharynx and assist with providing positive pressure on the bolus by contracting in a superior to inferior sequence (Donner, et al., 1985). While other muscles contract to facilitate pharyngeal shortening, the pharyngeal constrictor muscles are largely responsible for reducing the length of the pharyngeal segment. The orientation of fibres of the pharyngeal constrictors runs from superior at the posterior aspect to inferior at the anterior aspect. The resulting pressure on the bolus along with the narrowing and shortening of the pharyngeal lumen further facilitates pressure build-up in the pharynx.

**UES opening:** Initiation of UES relaxation is closely linked to activation of the submental muscles during hyolaryngeal excursion (Perlman, et al., 1999). The UES is a zone of high pressure that separates the pharynx from the esophagus. It comprises muscle fibres from the inferior pharyngeal constrictor muscle, the cricopharyngeus muscle, and some esophageal fibres (Belafsky, Rees, Allen, & Leonard, 2010). The cricopharyngeus muscle is tonically contracted during rest, preventing air from entering the gastrointestinal tract during

respiration, and gastric contents from entering the pharynx (Belafsky, et al., 2010; Hila, et al., 2001). Termination of the neural signal responsible for tonic contraction of the cricopharyngeus muscle results in relaxation (Ertekin & Aydogdu, 2003). This relaxation, combined with the traction force of hyolaryngeal excursion, results in UES opening during the swallow (Perlman & Christensen, 1997). Return of tonic contraction to the cricopharyngeus muscle is one of the final events in the pharyngeal swallow (Perlman, et al., 1999). The peak of UES opening has been shown to be almost synchronous with peak hyoid elevation (Crary, et al., 2006). UES opening is further facilitated by the direct pressure applied by the bolus as it passes through into the esophagus (Cook et al., 1992; Kahrilas, et al., 1996). Transport of the bolus through the UES is achieved by the pressure differential resulting from the traction force of laryngeal elevation in the closed oropharyngeal chamber (McConnel, et al., 1988). The increased pressure in the pharynx is met with negative pressure at the UES as it opens, resulting in a suction force on the descending bolus (McConnel, 1988). The UES is regarded as the 4<sup>th</sup> valve in the swallowing pressure system (Perlman & Christensen, 1997).

#### **2.1.4 Esophageal phase**

The esophageal phase begins as the tail of the bolus leaves the UES, and is much less complex than the preceding pharyngeal phase. The esophageal phase involves peristalsis of the striated (proximal) and smooth (distal) muscles of the esophageal wall to move the bolus through the lower esophageal sphincter into the stomach. The esophageal phase can take anywhere from 8-15 s (Miller, 1982).

### **2.2 Cranial nerves**

Cranial nerves (CNs) involved in swallowing typically consist of motor and/or sensory fibres (Figure 2.5). The motor fibres are responsible for transmission of the movement command from the nuclei in the brain to the oral, pharyngeal, and esophageal musculature. The sensory fibres are responsible for relaying sensation from the muscles and mucosal surfaces of the oral cavity and pharynx back to nuclei in the brain. The five cranial nerves, and combinations of spinal and cranial nerves, most heavily involved in swallowing are detailed below with their function in the swallowing process.

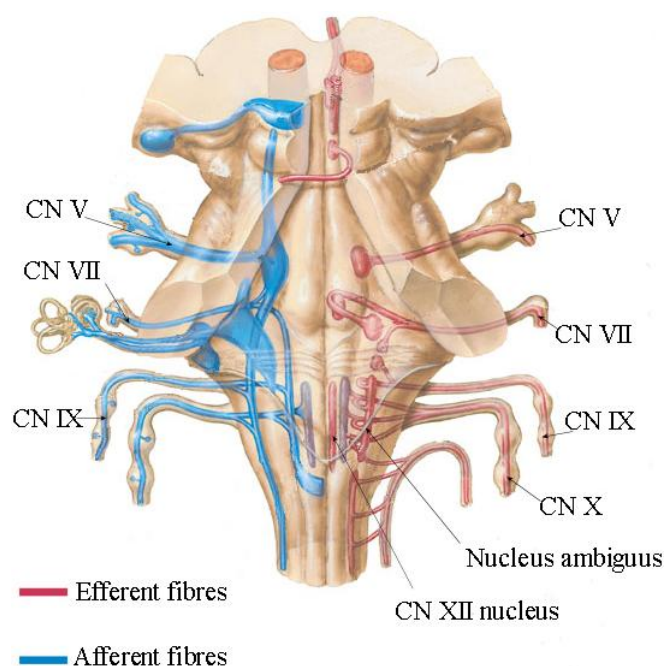


Figure 2.5<sup>5</sup> Cranial nerve nuclei in the brainstem.

### 2.2.1 Trigeminal nerve (CN V)

As its name suggests, the trigeminal nerve has three branches, each containing both motor and sensory fibres. The middle and lowermost branches of CN V, the maxillary and the mandibular branches respectively, are concerned with the control of swallowing (Perkins & Kent, 1986). Swallowing requires only sensory input from the maxillary branch but requires both sensory and motor input from the mandibular branch, (Perlman & Christensen, 1997). The sensory component of the maxillary branch carries information from the mucosal lining of the nasopharynx and palate, gums, and upper teeth (Perlman & Christensen, 1997). The motor component of the mandibular branch is primarily responsible for jaw opening and mastication. It innervates two of the three submental muscles (mylohyoid and anterior belly of the digastric muscles), which control jaw opening when the hyoid is fixed, and hyoid elevation when the jaw is fixed (Perlman & Christensen, 1997). The four muscles that are active during jaw closure and lateral jaw movement required for mastication (temporalis, masseter, medial pterygoid and lateral pterygoid) are also innervated by this branch (Perlman & Christensen, 1997). The sensory component of the mandibular branch carries sensation from the anterior two-thirds of the tongue, the mucosal lining of the cheeks and floor of

<sup>5</sup> Adapted from Netter, F. H. (1972). *Nervous System* (The Ciba Collection of Medical Illustrations. Vol. 1). New York: Ciba.

mouth, the gums, lower teeth, and skin of the lower lip and jaw (Perlman & Christensen, 1997).

In summary, the trigeminal nerve plays a major role in hyolaryngeal excursion due to its command over two of the three submental muscles. It is also responsible for jaw movements required for mastication, including opening, closing, and lateral movement. This nerve carries the sensory information for most of the oral structures and mucosa, suggesting its importance in communicating the whereabouts of the bolus to higher neural structures prior to the onset of swallowing.

### **2.2.2 Facial nerve (CN VII)**

The facial nerve contains both motor and sensory fibres. The motor fibres innervate the majority of the facial muscles, making facial movement and expression heavily dependent on this CN. Specific to swallowing, CN VII innervates the lips, which are considered the 1<sup>st</sup> valve of the swallowing system (Perlman & Christensen, 1997) and are also active during transfer of a bolus from a utensil. Accessory facial muscles (rizzorius, zygomaticus and quadratus labi superioris) that help to spread the lips for larger boluses are innervated by this nerve (Daniels & Huckabee, 2008). Motor fibres of the chorda tympani branch of CN VII are important for saliva production (Perlman & Christensen, 1997), through innervation of the submandibular and sublingual salivary glands (Daniels & Huckabee, 2008). Motor fibres also innervate muscles that assist with superior and posterior tongue positioning (Daniels & Huckabee, 2008; Perlman & Christensen, 1997), namely the stylohyoid and posterior belly of the digastric muscles. These muscles assist with glossopalatal seal during the oral phase of swallowing, and also with applying pressure to the bolus during transfer into the pharynx (Daniels & Huckabee, 2008). Another muscle pair recruited for swallowing innervated by CN VII is the buccinator muscles (Perlman & Christensen, 1997). The sensory component of the facial nerve plays a role in taste perception from the anterior two-thirds of the tongue (Perlman & Christensen, 1997) and the soft palate (Miller, 1999). Sensation from the soft palate and surrounding pharyngeal wall is also transmitted via the facial nerve (Daniels & Huckabee, 2008).

In summary, the facial nerve facilitates saliva production and taste and is responsible for obtaining and containing the bolus in the oral cavity through use of facial muscles. It also



assists with superior and posterior movement of the tongue for glossopalatal seal and bolus transfer.

### **2.2.3 Glossopharyngeal nerve (CN IX)**

The glossopharyngeal nerve functions alone, and in conjunction with CN X, to form the pharyngeal plexus (described below). The glossopharyngeal nerve in isolation provides motor control to only one muscle pair involved in swallowing, the stylopharyngeus muscles. This muscle pair is responsible for shortening and dilating the pharynx (Perlman & Christensen, 1997). Motor fibres also facilitate saliva production through innervation of the parotid salivary gland (Daniels & Huckabee, 2008). The sensory component of this nerve is responsible for sensation and taste perception for the posterior third of the tongue (Daniels & Huckabee, 2008). Sensory information from the mucosa of the oropharynx, the faucial arches and the palatine tonsils is also transmitted via this nerve (Perlman & Christensen, 1997), serving as a mechanism by which post-swallow residue is detected (Daniels & Huckabee, 2008).

In summary, CN IX has a primary function of taste and sensation to the posterior third of the tongue, and sensory receptors in the upper pharynx utilized to detect post-swallow residue which may require a clearing swallow. It facilitates pharyngeal shortening and dilates the pharynx during swallowing.

### **2.2.4 Vagus nerve (CN X)**

The deviations taken by this nerve over its course lead to its name, meaning ‘wanderer’ (Perkins & Kent, 1986). It is made up of many branches, two of which are integral for swallowing: the recurrent laryngeal nerve (RLN) and the superior laryngeal nerve (SLN). The RLN innervates all the intrinsic laryngeal muscles (Perlman & Christensen, 1997), including the interarytenoids and cricoarytenoids, both activated for vocal fold adduction prior to and during the swallow (Daniels & Huckabee, 2008). This nerve therefore innervates the 3<sup>rd</sup> valve of the swallowing pressure system, the larynx (Perlman & Christensen, 1997). Sensory fibres of the RLN also convey information from the tracheal bifurcation (Daniels & Huckabee, 2008), providing perception of material that has invaded the lungs. The SLN transmits sensation from more superior regions of the larynx and trachea (Daniels & Huckabee, 2008). This sensory transmission is important for airway protection by providing intra-swallow

feedback for activation of a reflexive cough response (see brainstem control of swallowing below) and providing post-swallow sensory feedback to facilitate clearing swallows. The rostral branch of the SLN is responsible for maintaining the tonic contraction in the cricopharyngeus muscle at rest (Daniels & Huckabee, 2008). This activation of the SLN is terminated during swallowing so the UES can be pulled open. This CN is therefore crucial to the function of the 4<sup>th</sup> valve in the pressure system: the UES (Perlman & Christensen, 1997).

In summary, components of the vagus nerve are integral in airway protection, using both motor control of laryngeal muscles to seal the airway and sensation of the mucosa of these muscles to detect airway invasion. It is also responsible for the contraction and relaxation of the cricopharyngeus muscle, which is the major component of the UES (Ertekin et al., 1995). This nerve controls two of the four valves that modulate pressure throughout the oropharyngeal cavity (Perlman & Christensen, 1997).

### **2.2.5 Pharyngeal plexus (CN IX, CN X)**

The innervation of swallowing musculature by the combination of CNs IX and X forms a crucial component of swallowing control, providing sensory and motor innervation to drive numerous swallowing events. It innervates the palatoglossus muscle, chiefly responsible for glossopalatal seal, and the glossopharyngeus muscle, which contracts to achieve contact between the base of tongue and the posterior pharyngeal wall (Daniels & Huckabee, 2008). It also innervates the levator veli palatine, which is recruited to accomplish velopharyngeal closure, the 2<sup>nd</sup> valve in the swallowing pressure system (Perlman & Christensen, 1997). The salpingopharyngeus and the palatopharyngeus, muscles involved in supraglottic shortening, are also innervated by pharyngeal plexus (Daniels & Huckabee, 2008). The other major contribution of the pharyngeal plexus is motor control to the superior, middle, and inferior constrictor muscles (Daniels & Huckabee, 2008), responsible for the superior to inferior squeeze on the bolus. Sensory feedback for the entire oropharynx and hypopharynx is also accomplished via the pharyngeal plexus (Daniels & Huckabee, 2008).

In summary, the pharyngeal plexus is important for the build-up of pressure in the pharynx through its role in sealing the velopharyngeal port, driving base of tongue contact with the posterior pharyngeal wall, shortening the pharyngeal lumen, and directing the top down squeeze of the pharyngeal constrictors. In addition, the sensory component is integral for safe

and efficient swallowing by conveying the location of the bolus in the pharynx both during and after a swallow.

### **2.2.6 Hypoglossal nerve (CN XII)**

Motor fibres of the hypoglossal nerve have primary responsibility for controlling tongue movement (Daniels & Huckabee, 2008; Perkins & Kent, 1986). CN XII innervates all of the intrinsic tongue muscles (transverse, longitudinal, and verticalis) and therefore has sole command over tongue contour (Daniels & Huckabee, 2008). The genioglossus, hyoglossus, and styloglossus all manipulate the position of the tongue within the oral cavity and are also innervated by this CN.

In summary, the hypoglossal nerve controls tongue movement and is, therefore, heavily relied upon for the oral phase of swallowing, as well as the propulsive action required from the tongue during transfer of the bolus into the pharynx.

### **2.2.7 Ansa cervicalis (CN XII, C1, C2)**

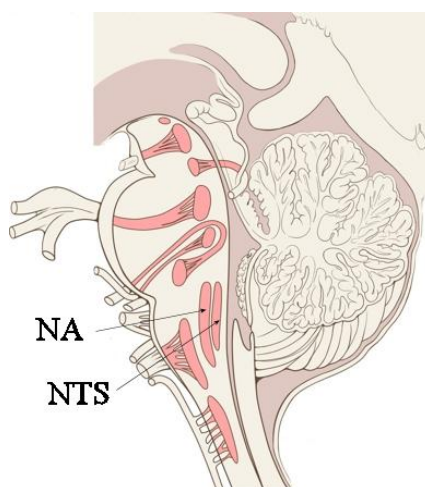
Ansa cervicalis is a combination of fibres from the hypoglossal nerve and the 1<sup>st</sup> and 2<sup>nd</sup> cervical spinal nerves (Bass & Morrell, 1992). There is disagreement in the literature regarding the components of ansa cervicalis (Daniels & Huckabee, 2008), with definitions varying regarding the inclusion of the hypoglossal nerve. Ansa cervicalis provides motor innervation for the remaining submental muscle pair (geniohyoid) and the strap muscles (omohyoid, sternohyoid, sternothyroid, thyrohyoid) (Curtis, Braham, Karr, Holborow, & Worman, 1988). Ansa cervicalis therefore contributes to hyolaryngeal excursion when the jaw is fixed through innervation of geniohyoid, and stabilizes the hyoid when jaw opening is required through innervation of the strap muscles.

## **2.3 Neural control of swallowing**

### **2.3.1 Brainstem control of swallowing**

The role of the brainstem in the neural control of swallowing is well documented and has been largely examined by microelectrode studies in animals (Jean, 1984a, 1984b; Jean & Car, 1979; Jean, Car, & Roman, 1975). Through these early studies, it was proposed that the complex movements involved in swallowing are shaped and organized by a central pattern

generator (CPG) housed in the medulla of the brainstem (Jean, 2001). The CPG consists of two main centres, both of which are represented bilaterally (Doty, Richmond, & Storey, 1967): the dorsal swallowing group (DSG), containing the nucleus tractus solitarius (NTS) (Figure 2.6) and the surrounding reticular formation, and the ventral swallowing group (VSG), containing the nucleus ambiguus (NA) and the surrounding reticular formation (Jean, 1984a; Jean & Car, 1979). It is generally accepted that the DSG is responsible for organization and integration of the movements for the basic swallowing pattern, and relies on input from cranial nerve afferents and the cortex for activation (Jean, 2001). The VSG contains the motor neurons responsible for distributing the motor command to the appropriate cranial nerves for activation of the oral, pharyngeal and esophageal muscles (Jean & Car, 1979). The activation of the VSG is dependent on the preceding activation of the DSG (Jean, 1984a), highlighting the organizational role of the DSG. The relatively fixed sequence of muscle activation seen in the pharyngeal swallow supports the theory that a centrally programmed pattern generator directs this motor command (Doty & Bosma, 1956; Perlman, et al., 1999).



*Figure 2.6<sup>6</sup>. Location of the nucleus tractus solitarius (NTS) and the nucleus ambiguus (NA) in the brainstem*

To confirm the function of the DSG and VSG, the specific components of the dorsal and ventral medulla and their functions should be considered. The NTS in the dorsal medulla contains the primary sensory nucleus for the facial, glossopharyngeal, and the vagus nerves (CN VII, IX and X) (Daniels & Huckabee, 2008). Afferent connections from the trigeminal

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<sup>6</sup> Adapted from [http://commons.wikimedia.org/wiki/File:Brain\\_stem\\_sagittal\\_section.svg](http://commons.wikimedia.org/wiki/File:Brain_stem_sagittal_section.svg) . Author: Patrick J. Lynch, medical illustrator License: Creative Commons Attribution 2.5 License 2006.

sensory nucleus in the pons are also evident in the DSG (Daniels & Huckabee, 2008). These links between the DSG and fibres carrying sensory information from the oral cavity, pharynx, and larynx highlight its role in integrating this information for subsequent initiation of the swallowing sequence. The NA contains the primary motor nucleus for the glossopharyngeal and vagus nerves (CN IX and X) (Bhatnagar & Andy, 1995). The NA also has efferent connections to the primary motor nucleus of the facial (Daniels & Huckabee, 2008) and trigeminal nerves in the pons (Amri, Car, & Jean, 1984), and the hypoglossal motor nucleus in the medulla (Amri & Car, 1988). The activation of these motor neurons following input from the DSG suggests the VSG translates the supplied motor plan to a command sequence for the cranial nerves innervating the swallowing musculature.

While the SLN of the vagus has its primary sensory nucleus in the NTS, it also has direct connections with the NA (Jean, 2001). This opportunity for sensory feedback from the larynx and trachea to bypass the NTS has been proposed as a means of inducing a reflexive cough response (Daniels & Huckabee, 2008). The direct link between the SLN and both the DSG and VSG most likely explain why swallowing is elicited with relative ease following stimulation of the SLN (Doty, et al., 1967).

Other areas of the brainstem are also involved in the control of swallowing. The motor and sensory nuclei of the trigeminal nerve are located in the pons (Dodds, 1989), with sensory connections to the DSG (Daniels & Huckabee, 2008), and motor connections from the VSG (Amri, et al., 1984). Afferent connections from the trigeminal sensory nucleus to the thalamus are also evident (Perlman & Christensen, 1997). The motor nucleus for the facial nerve (CN VII) is also located in the pons (Dodds, 1989) and receives efferent information from the VSG. It has been postulated that the neurons in the pons are a sensory relay for the SLN and glossopharyngeal nerve (Jean, et al., 1975). The trigeminal motor nucleus (in the pons) receives afferents from both the cortex and the trigeminal sensory nuclei (also in the pons), with the latter being responsible for relaying sensory information from a large proportion of the oropharynx (Perlman & Christensen, 1997). Evidence of these connections supports the notion of a pontine sensory relay to and from the cortex. The pontine neurons are therefore considered a major component of the mechanism responsible for providing sensory feedback to higher neural structures and also to the CPG in the medulla during a swallow (Jean, 2001; Jean, et al., 1975).

### **2.3.2 Cortical control of swallowing**

Unlike the brainstem, the role of the cerebral cortex in swallowing is not clearly understood (Kern, Jaradeh, Arndorfer, & Shaker, 2001). Cortical networks demonstrate potential for remodelling to at least partially compensate for damage (Buonomano & Merzenich, 1998; Duffau, 2006; Hamdy et al., 1996) and understanding this neural remodelling (or plasticity of the cortex) is considered imperative for improving the rehabilitation of disordered swallowing (Burkhead, Sapienza, & Rosenbek, 2007; Malandraki, Sutton, Perlman, Karampinos, & Conway, 2009; Martin, 2009; Robbins, et al., 2008). There has been a recent increase in literature documenting the contribution of the cerebral cortex and its networks to swallowing (Hiraoka, 2004; Huckabee, Deecke, Cannito, Gould, & Mayr, 2003; Humbert et al., 2009; Martin et al., 2007; Martin, Goodyear, Gati, & Menon, 2001; Martin et al., 2004; Martin & Sessle, 1993; Satow et al., 2004).

While historically the contribution of the cortex to the less volitional aspects of swallowing was in question, it is now generally accepted that modulation of the basic ‘patterned response’ swallow occurs at a cortical level (Robbins, et al., 2008). This theory is plausible as swallowing can be initiated volitionally without the need for airway protection or transfer of food through the pharynx (Jean, 2001). Furthermore, repetitive stimulation of specific parts of the cortex elicits a basic swallowing sequence (Jean & Car, 1979). Stimulation of the same areas of the cortex also activates ‘early’ neurons in the swallowing CPG (Jean & Car, 1979). These early neurons are seen to activate prior to other neurons and coincide with the onset of swallowing (Jean & Car, 1979). These neurons are active prior to initiation of swallowing, with activity increasing when swallowing is elicited, and decreasing when no swallowing occurs (Jean, 2001). The fact that stimulation of the cortex and cranial nerve afferents can induce similar activation in these neurons (Jean, 1984a) suggests summation of sensory and cortical inputs may be responsible for breaching the swallow ‘threshold’ of the CPG (Daniels & Huckabee, 2008). Reports of swallowing impairment following cortical stroke in the absence of brainstem damage further reinforces the necessity of the cortex beyond the volitional oral processes of swallowing (Meadows, 1973; Robbins & Levin, 1988). Additionally, the cortex houses the sensory nuclei of the olfactory and the optic nerve (CN I and II) (Daniels & Huckabee, 2008), confirming contribution from the cortex to pre-ingestive sensory modulation of smell and sight of the bolus.

Recent investigations using a variety of functional neuro-imaging techniques have sought to specify the contribution of cortical areas to the various swallowing processes. Functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG), positron emission tomography (PET), and event-related potentials (ERPs) are among the techniques used for these investigations. These studies have revealed that many regions of the cortex are activated during the swallowing process (Kern, et al., 2001; Mosier et al., 1999a; Mosier, Liu, Maldjian, Shah, & Modi, 1999b), with major contributions from the primary motor and sensory cortices (Dziewas et al., 2003; Hamdy et al., 1999a; Hamdy et al., 1999b; Humbert, et al., 2009; Kern, et al., 2001; Malandraki, et al., 2009; Martin, et al., 2001; Mosier, et al., 1999a), pre-motor and supplementary motor areas (Hamdy, et al., 1999a; Hamdy, et al., 1999b; Huckabee, et al., 2003; Humbert, et al., 2009; Malandraki, et al., 2009; Martin, et al., 2001), the anterior cingulate cortex (Hamdy, et al., 1999a; Kern, et al., 2001; Malandraki, et al., 2009; Martin, et al., 2001), insula (Dziewas, et al., 2003; Hamdy, et al., 1999a; Hamdy, et al., 1999b; Humbert, et al., 2009; Kern, et al., 2001; Malandraki, et al., 2009; Martin, et al., 2001), frontal operculum (Dziewas, et al., 2003; Hamdy, et al., 1999a; Humbert, et al., 2009; Malandraki, et al., 2009; Martin, et al., 2001) and the superior temporal gyrus (Dziewas, et al., 2003; Malandraki, et al., 2009; Martin, et al., 2001). The most consistent area of activation across various studies and swallowing tasks is the primary sensorimotor cortex (Ertekin & Aydogdu, 2003; Mosier, et al., 1999a). Included in the term ‘primary sensorimotor cortex’ for most studies are pre-motor cortex, supplementary motor area (SMA), the primary sensory cortex (S1), and primary motor cortex (M1). The SMA has frequently been identified as a major contributor to pre-motor planning of volitional movement (Ikeda, Luders, Burgess, & Shibasaki, 1992; Shibasaki et al., 1993). It has been suggested that SMA involvement is responsible, in part, for temporal, rather than spatial, coordination of sequential movements (Cunnington, Iansek, Bradshaw, & Phillips, 1995). The primary motor cortex is responsible for controlling motor movements of the contralateral side of the body (Bhatnagar & Andy, 1995). The primary sensory cortex integrates somatic sensation in the same manner (Bhatnagar & Andy, 1995).

Studies using electroencephalography (EEG) suggest a contribution from the SMA for volitional swallows (Hiraoka, 2004; Huckabee, et al., 2003; Satow, et al., 2004). However, the hypothesized function of this activation varies between studies, including factors such as motor preparation of oral movement (Satow, et al., 2004) and sensory feedback (Hiraoka,

2004). As none of these studies employed non-volitional swallowing conditions, the role of the SMA in more ‘reflexive’ response swallows cannot be deduced from previous EEG studies.

Activation of SMA, M1 and S1 during swallowing has been confirmed using fMRI (Hamdy, et al., 1999a; Humbert, et al., 2009; Kern, et al., 2001; Malandraki, et al., 2009; Martin, et al., 2001; Mosier, et al., 1999a). It has been suggested this involvement is largely due to the volitional aspects (such as the oral phase) of swallowing (Malandraki, et al., 2009). Opposing this belief, studies utilizing ‘reflexive’ swallowing conditions have shown activation is concentrated in the primary sensorimotor cortex for non-volitional swallowing (Kern, et al., 2001; Mosier, et al., 1999a). Reflexive swallowing is elicited by delivery of a bolus to the pharynx, eliminating volitional bolus manipulation and transfer. Attention to swallowing has also been controlled by keeping participants ignorant to the fact that swallowing was the task of interest, therefore eliciting naïve swallows (Martin, et al., 2001). Martin et al.’s study (2001) found M1 and pre-motor activation in the naïve condition but reduced activation in the anterior cingulate cortex, which is thought to represent pre-motor and/or attentional processing (Ertekin & Aydogdu, 2003; Kern, et al., 2001). This suggests fMRI outcomes were sensitive to differences in attention, signifying genuine M1 involvement in automatic swallow tasks.

fMRI has allowed researchers to identify specific neural regions activated during the swallowing process because it provides excellent spatial resolution of neural activation (Dziewas, et al., 2003). However, fMRI is very limited in temporal resolution. In particular, it cannot align neural regions with specific swallowing processes, as it lacks the temporal resolution needed to discretely analyse individual components or phases. The swallowing process involves motor planning, the volitional aspects of the oral preparatory stage, the reflexive components of the pharyngeal and esophageal phases and the sensory feedback that occurs throughout (Huckabee, et al., 2003). Reservations still remain regarding the contribution of the primary sensorimotor cortex in the more ‘reflexive’ swallowing components (Furlong et al., 2004). To understand which cortical regions are responsible for which swallowing processes each physiologic mechanism needs to be investigated in relative isolation (Malandraki, et al., 2009).



Attempts to alleviate the issue of poor temporal resolution associated with fMRI have been made by researchers employing MEG to assess cortical input during swallowing (Dziewas, et al., 2003; Furlong, et al., 2004). MEG allows greater temporal precision and therefore greater differentiation between the various swallowing events. A study by Furlong et al. (2004) showed activation of M1 when participants pressed their tongue to the roof of the mouth, a task considered to replicate oral preparation. M1 activation, along with SMA activation, was also shown during water infusion into the oral cavity. Consequently, the authors concluded that the primary sensorimotor cortex's role in the oral phase is largely concerned with processing sensory input from, and motor output to the tongue (Furlong, et al., 2004). Another study (Dziewas, et al., 2003) has provided more information for the debate regarding the role of the cortex in the more automatic pharyngeal phase of swallowing. This study incorporated a reflexive swallowing condition in which water was injected transnasally into the pharynx (Dziewas, et al., 2003). For a tongue press task and volitional swallowing, the areas of S1 and M1 corresponding to the tongue were activated, whereas for reflexive swallowing, the activated areas of S1 and M1 were located more medially (Dziewas, et al., 2003). Previous work by Hamdy and colleagues suggests medial activation represents more inferior muscles, such as those of the pharynx (Hamdy, et al., 1996).

A study using transcranial magnetic stimulation (TMS) of M1 to induce motor evoked potentials (MEPs) of the submental muscles revealed progressively larger MEPs from reflexive swallowing, to volitional swallowing, with volitional contraction of these muscles having the largest MEPs (Doeltgen, Ridding, Dalrymple-Alford, & Huckabee, 2011). The authors proposed that the decreased cortical input measured during the reflexive swallowing task reflected the increased level of brainstem control for this task compared with volitional swallowing and volitional contraction (Doeltgen, et al., 2011). As MEPs were still measurable during the reflexive swallowing task, this study offers further support for primary sensorimotor cortex input beyond the volitional components of swallowing, provided volitional preparation was adequately controlled in this study.

While cortical input for swallowing is uniformly described as bilateral (Mosier, et al., 1999a; Mosier, et al., 1999b), a general consensus exists that activation of the primary sensorimotor cortex is asymmetric (Hamdy, et al., 1999b; Mosier, et al., 1999a; Mosier, et al., 1999b). These findings have led to the term 'hemispheric dominance' for swallowing (Mosier, et al.,

1999b). Studies show this asymmetry varies from person to person (Humbert, et al., 2009; Martin, et al., 2001) and from task to task (Dziewas, et al., 2003; Kern, et al., 2001; Martin, et al., 2001), suggesting that hemispheric dominance cannot be inferred but must be assessed on an individual basis.

The collective evidence of the complex neural network involved in swallowing has led to the term ‘patterned response’ in favour of ‘reflex’, implying increased rehabilitative potential (Robbins, et al., 2008). Volitional control during swallowing may provide a gateway to modifying the patterned response, suggesting recruitment of the cortex is optimal for swallowing rehabilitation (Robbins, et al., 2008). It is likely that the cortex and CPG access the same pools of swallowing neurons (Ertekin et al., 2001a), reinforcing the possibility of accessing the patterned response by engaging the cortex with volitional swallowing. Furthermore, an override function of the cortex is implied from evidence that impairment of airway protection following anaesthesia of the pharynx and larynx can be overcome using voluntary manoeuvres (Jafari, et al., 2003). The early component of submental muscle contraction during volitional swallowing is thought to be under cortical control, while the later component is thought to be driven by the CPG (Ertekin & Aydogdu, 2003). It therefore reasons that increasing voluntary control over the leading complex of the pharyngeal phase may provide a link to modulate the patterned response. Evidence for the effects of swallowing therapies on cortical input during swallowing may help elucidate the most effective methods of overcoming disruptions in the patterned response that arise at a CPG level.

## **2.4 Dysphagia**

The term dysphagia is used to describe a disorder of swallowing. The word, of Greek origin, is a combination of ‘dys’ meaning disorder and ‘phagia’ meaning to eat (Cinocco, 2007). Swallowing impairment can result from damage to any of the muscles or neural regions involved in swallowing, or from disruption of the pathways connecting the two and is therefore a sequela of a vast array of medical diagnoses. Dysphagia can range from mild impairment, in which patients can maintain oral nutrition with occasional complaints of discomfort or coughing, to severe, with patients reliant on non-oral methods of nutrition and hydration.

### **2.4.1 Causes and incidence of dysphagia**

Congenital disorders, structural damage, or neurological insult can cause dysphagia, affecting individuals across the lifespan. Due to the array of medical diagnoses associated with dysphagia, it is difficult to obtain accurate incidence statistics. Exploring the common causes and the incidence of dysphagia within these populations provides the reader with an overall understanding of the extent to which dysphagia affects various individuals.

Many developmental disorders are associated with dysphagia. Progress in medical technology has seen an increase in the survival of children born prematurely and/or with low birth weight. These children often present with dysphagia as a result of either underdeveloped sensorimotor swallowing mechanisms or as a result of the common comorbidities associated with prematurity (Arvedson & Brodsky, 2002). As neurologic impairment resulting from abnormal prenatal brain development or birth trauma also impact on feeding ability, children with cerebral palsy frequently present with dysphagia (Morrell, 1992). Cleft palate, or other birth defects, may also produce dysphagia due to disruption of the structures and pressures required for effective suction in infants.

Acquired disorders such as stroke, head and neck cancer, traumatic brain injury, and neurodegenerative conditions are also associated with dysphagia. Dysphagia is an inevitable symptom for patients with Huntington's disease (Kagel & Leopold, 1992) as muscle coordination diminishes with progressive neuronal damage. Aspiration pneumonia is frequently the cause of death for patients with this disorder (Edmonds, 1966). An estimated 81% of patients with Parkinson's disease experience problems with swallowing, with duration and severity of disease being correlated with the presence of dysphagia (Coates & Bakheit, 1997). Various dementia types are also associated with dysphagia, with one study reporting 84% of dementia patients with some degree of swallowing complication (Horner, Alberts, Dawson, & Cook, 1994). It is estimated that around 30% of residents in long-term care facilities are fed non-orally, with a further 30% exhibiting clinical signs of dysphagia (Lin, Wu, Chen, Wang, & Chen, 2002).

As stroke is the leading cause of acquired dysphagia, statistics on stroke and the incidence of dysphagia within this group can provide insight into how many people are affected by the disorder. Approximately 6,000 new cases of stroke are documented in New Zealand each year (Stroke Foundation of New Zealand, 2010). When diagnosis is based on results of

instrumental examination, and heterogeneous stroke characteristics are included in the sample, the incidence of dysphagia is 78% (Daniels & Foundas, 1999). Taking into account lower values reported by other studies (Kidd, Lawson, Nesbitt, & Macmahon, 1993), a conservative estimate of 50% indicates approximately 3,000 individuals will be affected by dysphagia from stroke alone in New Zealand each year. With 57,700 adults reportedly living with the effects of a stroke (New Zealand Ministry of Health, 2008), approximately 28,850 New Zealanders are likely to have experienced dysphagia at some stage from this etiology alone. The large percentage of stroke patients affected by dysphagia reflects the complex interaction of many neural regions in swallowing control. Section 2.4.3 provides more detail regarding the common impairments of swallowing associated with stroke.

Recent research in the Auckland area has identified that Māori and Pacific Island people have a much higher incidence of stroke than their European counterparts and has increased by 66% over the past 20 years (Carter et al., 2006). This research also highlights that the average age of stroke is significantly younger in these populations, by an average of 10-15 years, indicating an increased risk of living with the effects of dysphagia in the Māori and Pacific island communities, and a need for improved outcomes for these populations.

## **2.4.2 Consequences of dysphagia**

The consequences of dysphagia are vast and result in substantially decreased quality of life (Sharp et al., 1999). Dysphagia is a predictor of mortality and is also associated with increased length of hospital stay, disability, and institutional care (Smithard et al., 1996). When the biomechanical processes involved in effective swallowing are disrupted, the design of the human anatomy predisposes patients to airway invasion from food and fluid. Figure 2.7 shows both a superior and lateral view of the entrance to the lungs and the entrance to the esophagus from the pharynx. This highlights the ease at which the airway can be compromised in the case of dysphagia, where protection of the airway during swallowing may be impaired. The term penetration is used to describe when the bolus infiltrates the airway to the level of the vocal cords or above. Aspiration is defined as invasion of the bolus into the airway below the level of the vocal cords, posing a greater risk for pulmonary compromise than penetration. Aspiration in and of itself is not overly hazardous and occurs frequently in both healthy and disordered populations, often with no adverse consequences (Bartlett & Gorbach, 1975). When combined with other risk factors, frequent aspiration of large amounts

impairs the efficacy of clearance mechanisms of the lungs, often resulting in an infection known as aspiration pneumonia. A study by Langmore and colleagues (1998) highlights the interaction of various risk factors in causing aspiration pneumonia. This report suggests that predictors include dependence for feeding, dependence for oral care, tube-feeding, more than one medical diagnosis, and multiple medications (Langmore, et al., 1998).

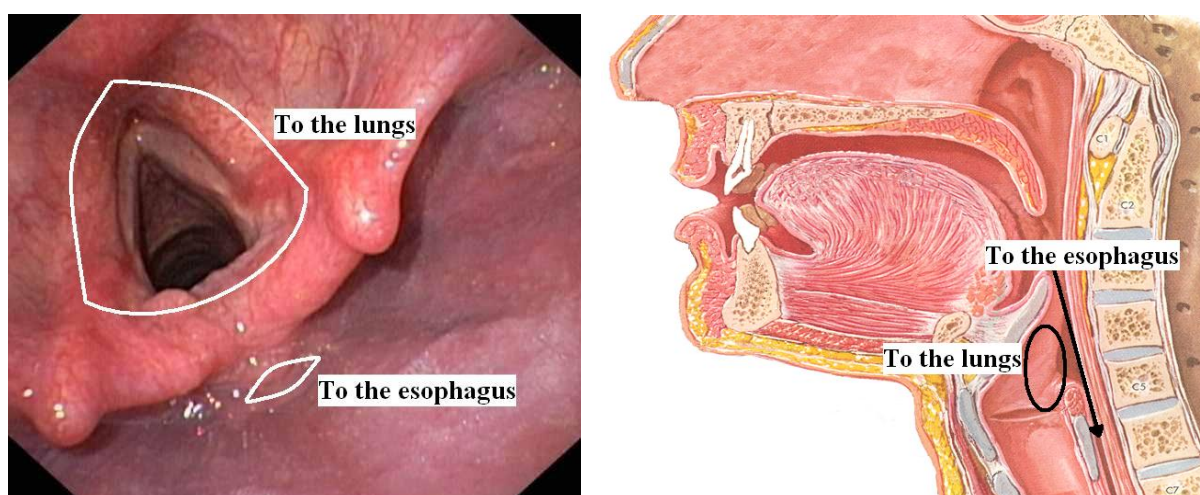


Figure 2.7. Superior (left) and lateral (right) view of the laryngeal entrance and esophageal entrance (UES). The laryngeal entrance is larger and sits open at rest, while the UES sits closed at rest.

Aspiration pneumonia complicates recovery for as many as 47% of stroke patients (Upadya, Thorevska, Sena, Manthous, & Amoateng-Adjepong, 2004), and is responsible for a large proportion of infections in nursing home patients (Langmore, et al., 1998). Research has shown pneumonia resulting from aspiration to be the most common cause of ‘bounce-back’ admissions to hospital (re-admission within 30 days of discharge) (Kind, Smith, Pandhi, Frytak, & Finch, 2007), suggesting the cost of treatment is substantial for healthcare systems. However, the ultimate cost is met by many patients, with aspiration pneumonia being a leading cause of death in the acute phase following stroke (Aslanyan, Weir, Diener, Kaste, & Lees, 2004; Marik, 2001).

Aspiration and consequent pulmonary compromise are not the only adverse outcomes of dysphagia. With the transport of food and fluid from the mouth into the esophagus compromised, dehydration and malnutrition are common consequences of dysphagia (Aslanyan, et al., 2004; Marik, 2001). Malnourishment has been associated with increased length of hospital stay and decreased functional improvement (Finestone, Greene-Finestone,

Wilson, & Teasell, 1996). Malnutrition and dehydration are associated with infection, confusion, impaired wound healing, depression, increased morbidity, and hip fractures in the elderly (Greene Burger, Kayser-Jones, & Prince, 2000), highlighting the importance of dysphagia management in this population.

While medical status is often compromised in patients with dysphagia, psychosocial effects are also associated with this impairment (Nguyen et al., 2005). The severity of dysphagia is correlated with reduced quality of life scores, anxiety, and depression (Nguyen et al., 2005), suggesting a need for intervention even in patients whose medical status may be relatively stable.

### **2.4.3 Pathophysiology of dysphagia**

Physiologic impairment of the oral phase of swallowing often involves reduced oral motor efficiency, characterized by deficits of strength, range of motion and flexibility. Disruption to the function of the oral muscles may manifest as an inability to prepare, control, and transport the bolus into the pharynx. Due to the more voluntary nature of the oral phase, impairments are common with cortical damage (Massey & Shaker, 2006), however lower motor neuron damage from brain stem injury may also produce oral phase deficits. Disorders of the oral phase have been shown to contribute to aspiration in approximately 80% of cases (Feinberg & Ekberg, 1991), highlighting the importance of this phase for maintaining pulmonary integrity. These findings reinforce the significant influence of the oral phase on the ensuing pharyngeal response. The sensory information relayed from the oral structures, combined with the cortical information generated during this phase are critical inputs for evoking the patterned pharyngeal response at the brainstem central pattern generator (Daniels & Huckabee, 2008). Disorders of the oral phase can therefore also impair the initiation of the swallowing response (Massey & Shaker, 2006).

Because of the rapid and precise combination of events required in the pharyngeal phase, minimal deviations in spatial or temporal coordination can substantially disrupt the efficacy of this phase. Lesions of the brainstem frequently disrupt the efficacy of the pharyngeal phase (Huckabee & Pelletier, 1999) due to the role of the brainstem in initiating and supplying the motor command for the pharyngeal swallow response. Common physiologic abnormalities seen in patients with pharyngeal phase deficit include reduced hyolaryngeal excursion,

reduced or dyscoordinated pharyngeal contraction, and inadequate airway protection. The biomechanical events reliant on hyolaryngeal excursion make such impairment detrimental to the effective passageway of the bolus through the pharynx. The contribution of epiglottic deflection to airway protection, and the crucial role of the UES in bolus transfer are both potentially compromised when hyolaryngeal is diminished, making this deficit a common cause of pharyngeal phase dysphagia. Pharyngeal phase impairments have been shown to contribute to aspiration in approximately 55% of cases (Feinberg & Ekberg, 1991).

#### **2.4.4 Treatment of dysphagia**

A number of compensatory and rehabilitative manoeuvres have been developed to manage disorders of swallowing. The need to treat the acute presentation of dysphagia has traditionally been the driving force for development of treatments. Thus, techniques have typically emerged into clinical practice ahead of supportive, empirical evidence for them (Langmore, 1995; Robbins, et al., 2008; Rosenbek, 1995). Furthermore, many techniques were designed to immediately address symptoms of dysphagia rather than address physiologic deficits, therefore providing only transient compensatory relief from the burden of impairment. Providing empirical evidence of treatment effects presents an enormous challenge for researchers, as the complexity of swallowing makes documenting all treatment modifications that take place problematic. Adding to the challenge is the heterogeneity of impairment aetiologies and the large number of swallowing components that can be affected, even in homogeneous patient groups. This heterogeneity makes it difficult to specify which physiologic impairments respond positively to certain treatment techniques. Despite these limitations, researchers are increasingly providing empirical evidence for commonly used treatments. Additionally, the necessity for such evidence prior to the widespread use of novel techniques is now generally accepted. This evidence is essential to provide the much-needed support for clinical management of dysphagia.

When impairments of the oral phase are due to neurological disruption, such as stroke, it seems logical to assume that the cortical nature of this phase may render it responsive to volitional rehabilitation manoeuvres. There is a surprising scarcity of literature providing evidence for such rehabilitation. However, a series of studies investigating the effects of tongue-to-palate strengthening exercises in healthy subjects (Lazarus, Logemann, Huang, & Rademaker, 2003; Robbins et al., 2005) and, more importantly, dysphagic patients (Robbins

et al., 2007) suggest that this type of rehabilitation may be effective for functional improvement of swallowing. When deficits arise as a result of impaired anatomy, such as in the case of head and neck cancers, the debilitating effects may be more chronic in nature, requiring compensatory management techniques.

As with any phase of swallowing, the root of impairment in the pharyngeal phase can be sensory or motor. If sensory deficits prevent the initiation of pharyngeal swallowing, the ensuing cascade of biomechanical events is also inhibited. In this case, sensory-based treatments such as thermal or tactile stimulation are utilized in an attempt to prompt the swallowing response. If motor impairments reduce the magnitude of specific biomechanical events in the pharyngeal phase, the typical approach is to strengthen the impaired component, through techniques such as the head-lift manoeuvre or effortful-swallowing. The impairments seen frequently in patients with pharyngeal phase dysphagia (see Section 2.4.3) are commonly targeted by rehabilitation techniques which aim to strengthen or prompt the initiation of these biomechanical processes. Treatment of pharyngeal phase impairment presents a challenge for clinicians, as the process of gaining access to the patterned response through volition is not clearly understood. Furthermore, many biomechanical events happen in rapid succession within the pharynx, a chamber unable to be visualized freely for guided feedback or modulation. Therefore, empirical evidence is crucial for clinicians attempting to remedy the complexities of pharyngeal phase swallowing impairments, and to assist with eliminating the burden of dysphagia. Chapter 10 provides a more in-depth review of empirical evidence for dysphagia rehabilitation.

## **2.5 Summary**

Dysphagia is a common sequela of neurological insult and disease. The consequences of dysphagia reduce quality of life, increase the risk of medical complications and mortality, and pose a substantial cost to healthcare systems. Effective rehabilitation of dysphagia is required to effectively manage this disorder. As swallowing is one of the most complex neuromuscular tasks executed by humans, deciphering the optimal methods for rehabilitating the biomechanical and neural mechanisms in the case of impairment presents an immense task. It is known that neural and functional recovery can occur following neurological insult, and understanding this process is imperative for the management of dysphagic patients. The crucial role of empirical evidence in guiding swallowing rehabilitation is now widely



accepted. Commonly prescribed treatments now require thorough scientific evaluation to strengthen, justify, or, indeed, contraindicate their use for treatment of swallowing impairment.



## **PART II: METHODOLOGICAL STUDIES**



## Chapter 3: Literature review – Measuring change in swallowing

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There are numerous techniques available for assessing swallowing with the choice of measure dependent on the goal of the investigation. The technique commonly referred to as the ‘gold standard’ for diagnostic assessment of swallowing is the videofluoroscopic swallowing study (VFSS) (Rugiu, 2007). VFSS provides two-dimensional dynamic evaluation of all phases of swallowing. Another commonly used clinical assessment tool is fiberoptic endoscopic evaluation of swallowing safety (FEES), which provides direct, three-dimensional images of the upper digestive tract (Langmore, Schatz, & Olsen, 1988). The information provided by these two assessment tools is vastly different. Specifically, the dynamic view of all phases of swallowing achieved with VFSS means it is commonly the tool of choice for assessing overall structural integrity and biomechanics associated with swallowing function. FEES is limited to investigation of the pharyngeal phase of swallowing, with its strength being in the assessment of airway protection mechanisms prior to and following the swallow (Langmore, et al., 1988). During the peak of the pharyngeal swallow, the image is obliterated due to light reflecting back into the camera from swallowing structures (Rugiu, 2007), therefore evaluation of swallowing dynamics is limited with FEES (Langmore, et al., 1988). While specific swallowing components can be quantified (such as VFSS for hyolaryngeal excursion, see Section 3.4.1), this process often involves complex data calibration and transformation. Therefore interpretation of both measures in clinical diagnostics is based largely on subjective and qualitative description. For this reason, the strengths of these diagnostic assessments do not easily translate to research, where accurate quantification of swallowing biomechanics is required.

The limited research application of these methods is supported by studies assessing the intra- and inter-rater reliability of VFSS interpretation in experienced speech and language therapists utilizing standardized evaluation protocols (Kuhlemeier, Yates, & Palmer, 1998; Stoeckli, Huisman, Seifert, & Martin-Harris, 2003). These studies have concluded that aspiration or penetration of texture into the airway, a relatively well defined and easily visualized event, is the only swallowing event to be rated with adequate reliability (Kuhlemeier, et al., 1998; Stoeckli, et al., 2003). The interpretation of all other swallowing parameters, including all pharyngeal phase components, varies greatly within and between raters. While both VFSS and FEES have a critical role in diagnosing and defining physiologic impairments in the case of dysphagia, their use for quantitative assessment of

healthy populations in which the effects of treatments may be quite subtle is likely to be limited.

The many biomechanical events which are so rapidly completed during swallowing (see Section 2.1) require researchers to employ quantitative outcomes measures, determined by logical assessment of what biomechanical events are likely to be influenced by the treatments being investigated. Many researchers develop novel quantitative measures, such as transit times of the bolus between various structures (Fraser et al., 2002; Jefferson et al., 2009a; Mistry et al., 2007; Power et al., 2004), and ratios of the size or movement of various structures (Leonard, Belafsky, & Rees, 2006), measured with methods such as VFSS, ultrasound, and manometry. As FEES does not allow visualization of most biomechanical swallowing events, such as hyolaryngeal excursion, its application is typically reserved for specific assessment of airway compromise in dysphagic patients. VFSS exposes participants to ionizing radiation, a process that is ethically difficult to justify in the case of non-impaired participants. The limitations of these two commonly used assessment tools render them unsuitable for research of healthy participants, therefore their clinical application is not discussed. This chapter will provide an overview of some of the instrumental measures used to quantify swallowing parameters for research, discussing the limitations and strengths of each in an attempt to provide the reader with insight into how these research methods contribute to the assessment of overall swallowing function.

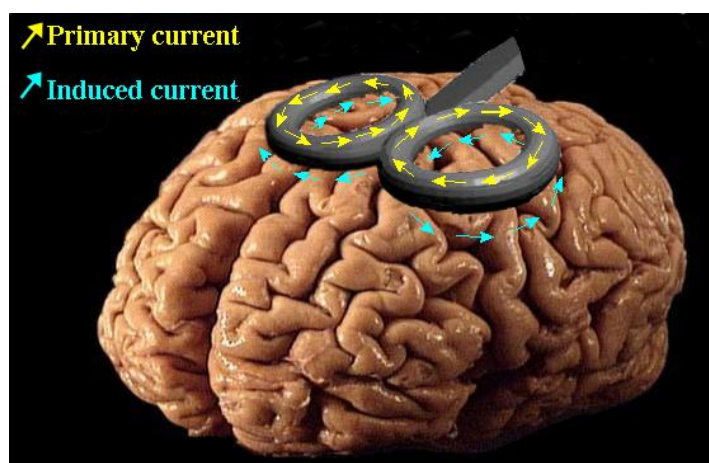
### **3.1 Cortical and corticobulbar function**

Neural processes associated with swallowing can be measured with a number of functional imaging techniques, including fMRI, EEG, MEG, PET, and single photon emission computed tomography (SPECT). Many investigations of neural function related to swallowing recovery have utilized TMS to induce MEPs of various swallowing muscles. This method of documenting corticomotor function is discussed in more detail below.

#### **3.1.1 Transcranial magnetic stimulation**

TMS was first described by Barker et al. (1985) as a non-invasive technique for stimulating the motor cortex in humans. To determine conduction time and excitability of corticobulbar or corticospinal projections, an electrical impulse is generated by the discharge of a high electrical current through an external coil held parallel to the scalp surface and overlying the

motor cortex. This current induces a transient magnetic field perpendicular to the coil (Hallett, 2000) which penetrates the scalp, skull, and brain tissue. This changing magnetic field, in turn, induces a circulating ‘eddy’, or secondary, electrical current perpendicular to the magnetic field and, therefore, parallel to the primary electric current, but in the opposite direction to that in the coil (Epstein, 2008) (Figure 3.1). The intermediary magnetic field means that the electric current is induced in the underlying brain with minimal sensation and minimal attenuation of the magnetic field (Barker, 1999).



*Figure 3.1. Schematic of the current induced in the underlying brain from transcranial magnetic stimulation<sup>7</sup>.*

Cell bodies, axons, and dendrites within the brain are hyperpolarized at points where the current enters and are depolarized at points where the current exits (Mills, 1999). The point of depolarization (or point of stimulation) is where the current exits the stimulated fibre, typically where the fibre bends away from the current, or where the current bends away from the fibre, or at points of diameter change, such as the transition from cell body to axon (Mills, 1999). A propagating action potential will be initiated if the depolarization exceeds the activation threshold (Mills, 1999). Axons have lower thresholds than cell bodies or dendrites (Ranck, 1975) and are the most likely location of initiation of an action potential in cortical interneurons (Salvador, Silva, Basser, & Miranda, 2011). Additionally, magnetic stimulation preferentially activates fibres that lie parallel to the stimulating coil (usually parallel to the brain surface) such as intracortical fibres, rather than perpendicularly-oriented pyramidal

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<sup>7</sup> Adapted from <http://goodliffe.blogspot.com/2010/04/learning-understanding-brain.html>

neurons (Kapogiannis & Wassermann, 2008; Rothwell, 1997; Stefan, Kunesch, Cohen, Benecke, & Classen, 2000).

### **3.1.1.1 TMS induced Motor evoked potentials**

The MEP (measured by electromyography [EMG]) is the resulting electrical potential that signifies the muscle's response to stimulation of the corticobulbar or corticospinal pathways (Griskova, Hoppner, Ruksenas, & Dapsys, 2006). The MEP represents the muscle activity brought about by temporal and spatial summation of direct (D) and indirect (I) waves in the spinal or bulbar segment, which activates the corresponding alpha motor neurons (Kapogiannis & Wassermann, 2008; Lissens, 2003). D- and I-waves have been measured with an electrode on the medullary pyramid or the spinal cord, and represent the repetitive firing of the pyramidal neurons in response to exogenous stimulation, from either direct (D-wave), or transynaptic activation (I-waves) (Di Lazzaro, 2008). The latency of D-waves is shorter than that of I-waves, reflecting the increased number of synapses travelled by the latter. TMS typically evokes I-waves (Rothwell, 1997; Terao & Ugawa, 2002), due to its preferential activation of corticocortical fibres that transynaptically activate the pyramidal neurons. D-waves are usually detected in response to electrical stimulation, or at high intensities of magnetic stimulation (Di Lazzaro, 2008). The MEP therefore reflects the accumulation of motor neuron activations resulting from the summation of I-waves. Desynchronization of motor neuron discharges can result in phase cancellation, or the neutralization of electric potential due to the negative phase of one motor unit coinciding with the positive phase of another (Rosler & Magistris, 2008). The MEP is an amalgamation of potentials and therefore incorporates this inherent phase cancellation, which explains, in part, the large trial-to-trial variability in MEP measures (Darling, Wolf, & Butler, 2006; Ellaway et al., 1998; Thickbroom, Byrnes, & Mastaglia, 1999).

The response latency of the MEP (Figure 3.2) represents the time from initiation of motor cortex stimulation to the first sign of the associated EMG response in the peripheral muscle (Hamdy, Aziz, Rothwell, Hobson, & Thompson, 1998a). The amplitude of the MEP (Figure 3.2) represents the level of excitation of the corresponding pathways between the motor cortex and the peripheral muscle (Chen, 2000). Amplitude of MEP is calculated as the largest distance between consecutive positive and negative peaks, or as area of the rectified MEP, and thus influenced by the duration of the EMG response. MEP amplitude reflects the state of

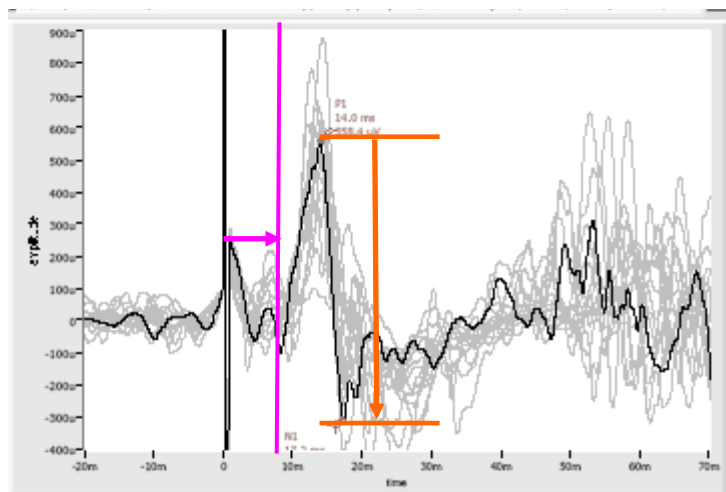


the excitatory corticocortical axons, corticospinal or corticobulbar neurons, spinal or bulbar motor neurons, and muscle fibres, as well as the effectiveness of the intermediary excitatory synapses (Kapogiannis & Wassermann, 2008). Excitatory and inhibitory inputs to each neuron along this pathway determine its efficiency in transmitting excitatory activity (Kapogiannis & Wassermann, 2008). Therefore MEP amplitude signifies the overall excitability of the corticomotor system being investigated. Despite the contribution of multiple neurons and synapses to the MEP, when stimulating parameters remain unchanged, increases in MEP amplitudes are considered to reflect greater excitability in the corticocortical neurons rather than subcortical structures (Devlin & Watkins, 2008; Fraser, et al., 2002). This is based on studies that document less variable EMG responses when stimulation occurs at structures further along the corticomotor pathway than the motor cortex (Kiers, Cros, Chiappa, & Fang, 1993; Moosavi, Ellaway, Catley, Stokes, & Haque, 1999). Changes in MEP latency suggest alterations in the conduction time of the neural command from the motor cortex to the muscle (Chen, 2000; Misulis, 1994), through more or less rapid depolarization of neurons within the corresponding pathway. MEPs recorded from proximal muscles often exhibit shorter response latencies than those recorded from distal muscles, reflecting reduced distance between the cortex and motor unit in the former.

Imaging techniques such as fMRI (Fraser, et al., 2002) and MEG (Gow, Hobson, Furlong, & Hamdy, 2004a) have been utilized to validate changes in MEP amplitudes with changes in underlying neural processes. Increased MEP amplitude has been shown to coincide with increased activation in the sensorimotor cortex as seen in fMRI (Fraser, et al., 2002) and MEG (Gow, et al., 2004a), signifying that MEPs measured at the muscles of swallowing represent cortical changes documented with other imaging techniques.

Various measures of motor physiology can be obtained using TMS-induced MEPs, including motor threshold and cortical muscle representation maps (Chen, 2000). Motor threshold is defined as the lowest stimulus intensity required to elicit an MEP of pre-defined size, usually around 50  $\mu$ V for limb muscles (Chen, 2000) and 20  $\mu$ V for swallowing muscles (Fraser et al., 2003; Gow, et al., 2004a; Mistry, Rothwell, Thompson, & Hamdy, 2006; Mistry, et al., 2007). Cortical muscle representation maps involve discharging the magnetic stimulation over numerous adjacent points on the motor cortex and documenting the number of points that register a MEP in the muscle(s) of interest (Chen, 2000). Another pertinent component of the

cortical map is the site eliciting the largest MEP in the target muscle(s), commonly referred to as the “hot spot” (Mistry, et al., 2007; Plowman-Prine, Triggs, Malcolm, & Rosenbek, 2008). The hotspot is the location on the scalp that presumably accesses the greatest amount of cortical projections to the target muscle when stimulated (Butler & Wolf, 2003).



*Figure 3.2. MEP onset latency and peak-to-peak amplitude. The pink arrow represents the time (in ms) from magnetic stimulus (solid black line) to onset of MEP (solid pink line). The orange arrow represents the peak-to-peak amplitude (in  $\mu V$ ).*

### **3.1.1.2 MEPs from muscles involved in swallowing**

MEP recordings have high temporal resolution (Ilmoniemi, 2002) and, therefore, have the temporal sensitivity to detect neural changes that occur with the swallowing process. TMS has been used for cortical mapping (Gallas, Marie, Leroi, & Verin, 2009; Hamdy, et al., 1996; Khedr et al., 2008; Oh, Kim, & Paik, 2007; Plowman-Prine, et al., 2008) and quantification of MEPs from submental muscles (Doeltgen, et al., 2010a; Doeltgen, Ridding, O'Beirne, Dalrymple-Alford, & Huckabee, 2009a; Gallas, et al., 2009; Gallas et al., 2007; Hamdy et al., 1997; Plowman-Prine, et al., 2008), pharyngeal muscles (Fraser, et al., 2002; Fraser, et al., 2003; Gow, et al., 2004a; Gow, Rothwell, Hobson, Thompson, & Hamdy, 2004b; Hamdy, et al., 1997; Hamdy, et al., 1998a; Hamdy, et al., 1996; Jefferson, et al., 2009a; Jefferson, Mistry, Singh, Rothwell, & Hamdy, 2009b; Mistry, et al., 2006; Mistry, et al., 2007; Plowman-Prine, et al., 2008; Power, et al., 2004), esophageal muscles (Ertekin et al., 2001b; Fraser, et al., 2003; Hamdy, et al., 1996; Khedr, et al., 2008; Khedr, Abo-Elfetoh, & Rothwell, 2009) and other swallowing muscles (Ertekin, et al., 2001b). These studies have shed light on many pertinent issues relating to plasticity of corticomotor function associated

with swallowing, including differential hemispheric contribution to swallowing (Hamdy et al., 1998b; Hamdy, et al., 1996), recovery of dysphagia following stroke (Hamdy, et al., 1996), and the effects of rehabilitation techniques on cortical excitability (Doeltgen, et al., 2010a; Fraser, et al., 2002; Fraser, et al., 2003; Gow, et al., 2004a; Gow, et al., 2004b; Hamdy, et al., 1997; Hamdy, et al., 1998a; Jefferson, et al., 2009a; Jefferson, et al., 2009b; Khedr, et al., 2009; Mistry, et al., 2006; Mistry, et al., 2007; Power, et al., 2004).

Insight into rehabilitation effects has been offered by studies using MEPs to show excitatory effects (Doeltgen, et al., 2010a; Fraser, et al., 2002; Fraser, et al., 2003; Gow, et al., 2004a; Gow, et al., 2004b; Hamdy, et al., 1997; Hamdy, et al., 1998a; Jefferson, et al., 2009a; Jefferson, et al., 2009b; Khedr, et al., 2009; Mistry, et al., 2006; Mistry, et al., 2007; Power, et al., 2004) and inhibitory effects (Fraser, et al., 2003; Jefferson, et al., 2009b; Mistry, et al., 2006; Mistry, et al., 2007; Power, et al., 2004) of treatment techniques on swallowing neural pathways. An increase in MEP amplitude has been documented following treatment protocols including repetitive transcranial magnetic stimulation (rTMS) (Gow, et al., 2004b; Jefferson, et al., 2009a; Khedr, et al., 2008; Khedr, et al., 2009), transcranial direct current stimulation (tDCS) (Jefferson, et al., 2009b), neuromuscular electrical stimulation (NMES) (Doeltgen, et al., 2010a; Fraser, et al., 2002; Fraser, et al., 2003; Gow, et al., 2004a; Hamdy, et al., 1998a; Power, et al., 2004), cranial nerve stimulation (Hamdy, et al., 1997; Hamdy, et al., 1998a), task-oriented swallowing exercises (Fraser, et al., 2003) and non-task-oriented swallowing exercise (Gallas, et al., 2009).

Many studies which document changes in corticomotor excitability as a result of treatment paradigms have done so using healthy participants (Doeltgen, et al., 2010a; Fraser, et al., 2003; Gow, et al., 2004a; Gow, et al., 2004b; Hamdy, et al., 1997; Jefferson, et al., 2009a; Jefferson, et al., 2009b). While many of these studies have not utilized control conditions, some have employed sham conditions to show that changes in corticomotor excitability are specific to the treatment being applied (Gow, et al., 2004a; Jefferson, et al., 2009a; Jefferson, et al., 2009b). Studies have frequently utilized MEPs from healthy participants to determine optimal treatment parameters for patient populations, but unfortunately have not extended the investigation of MEPs to patients (Power et al., 2006). Only two studies have examined changes in corticobulbar excitability as a result of intervention using dysphagic patients (Fraser, et al., 2002; Khedr, et al., 2009). One study investigated changes in excitability of

cortical projections to the esophagus following rTMS (Khedr, et al., 2009), and the other at the effect of electrical stimulation on projections to the pharynx (Fraser, et al., 2002). Both studies employed sham conditions in an attempt to control for differences unrelated to treatment. Unfortunately, the sham group in the study by Khedr and colleagues did not participate in the outcome MEP assessment, and therefore the comparison between groups was not possible. The study by Fraser and colleagues is therefore the only study of changes in cortical excitability as a result of treatment utilizing a control group for comparison. However, by contrasting the results of the study by Khedr and colleagues with those that have utilized the same treatment in healthy participants, some insight can be gained into the response of impaired corticobulbar pathways to rehabilitation as measured with MEPs.

Three studies investigating the effects of rTMS on healthy participants (Gow, et al., 2004b; Jefferson, et al., 2009a; Mistry, et al., 2007) can be compared with the study of dysphagic patients by Khedr and colleagues. The studies of healthy participants found that 5 Hz rTMS, generally accepted as an excitatory paradigm, increased the excitability of cortical projections to the pharynx (Gow, et al., 2004b; Jefferson, et al., 2009a), and 1 Hz rTMS, generally accepted as an inhibitory paradigm, decreased the excitability of the same projections (Jefferson, et al., 2009a; Mistry, et al., 2007). Additionally, when 1 Hz rTMS was followed with 5 Hz rTMS, the initial depression in cortical excitability seen after 1 Hz stimulation was reversed, as demonstrated by increased MEP amplitudes (Jefferson, et al., 2009a). Interhemispheric influences on projections to the swallowing muscles have been reinforced following the observation that MEPs elicited from both the stimulated and non-stimulated hemisphere increase after excitatory paradigms (Gow, et al., 2004b; Jefferson, et al., 2009a). Khedr and colleagues (2009) revealed a similar bilateral hemispheric increase in corticobulbar projections to the esophagus in dysphagic patients following rTMS. These similarities suggest that the response of the corticobulbar pathway to treatments measured with MEPs may be similar in patients and healthy controls.

However, there are limitations in making direct comparisons between the MEP response from healthy participants and dysphagic patients from this series of studies. Firstly, the study of dysphagic patients measures excitability of projections to a different muscle group (i.e., the esophagus) than the studies of healthy participants, which investigate pharyngeal projections. The cortical inputs and modulation of these inputs may differ between the esophagus and the

pharynx based on the lack of volition involved esophageal peristalsis. Additionally, Khedr and colleagues employ different rTMS stimulation parameters to the studies of healthy participants, utilizing 3 Hz rather than 5 or 1 Hz, as well as different quantities and duration of stimulation pulses. As changes in excitability of cortical projections from the same location have been shown to be frequency specific (Gow, et al., 2004b), intensity specific (Mistry, et al., 2007), and duration specific (Jefferson, et al., 2009a), the comparison of these studies is limited. Clearly it is unfortunate that the sham group in Khedr and colleagues' study was unable to complete the MEP measures (Khedr, et al., 2009). Because factors unrelated to treatment were not controlled, and because this study included patients within the acute phase post-stroke (2 weeks), the confounding factors associated with recovery cannot be discounted as responsible for changes in corticobulbar excitability. Regardless of the cause of change in MEPs, the coincident improvement in blinded clinical ratings of dysphagia documented by Khedr (2009) may offer some insight into corticomotor adaptations associated with improved swallowing function as a result of treatment.

The single study of corticomotor response to electrical stimulation of the pharynx in dysphagic patients includes a sham condition offering greater insight into how modifications in patients may be influenced by treatment (Fraser, et al., 2002). Despite the authors' report of real stimulation having a "larger effect on response amplitudes and map areas" than the sham condition, the difference did not reach statistical significance. The significant improvement in swallowing function and aspiration scores documented for the real-stimulation group but not the sham group may suggest functional improvements were not accompanied by changes in corticomotor excitability. However, there are methodological limitations with this study preventing such conclusions. Firstly the authors do not report blinded assessment of swallowing function, suggesting researcher bias may be responsible for improvements. This is especially concerning given the authors discuss the trend of increased MEP amplitudes as a genuine effect of treatment. Additionally, many of their functional outcome measures were subjectively determined. Finally, patients were in the acute phase post-stroke, with a larger number being assigned to the real-stimulation group, suggesting spontaneous recovery cannot be excluded as the cause of improvements. While the limitations of this study do not provide insight into patient corticobulbar response to treatment, it shows that excitability of projections from the unaffected hemisphere in dysphagic patients is increased to a greater extent following treatment than the affected hemisphere. This finding supports previous

research showing that recovery of dysphagia is associated with plasticity of the unaffected hemisphere (Barritt & Smithard, 2009; Hamdy, et al., 1998b; Hamdy, Rothwell, Aziz, & Thompson, 2000). The fact that only two studies have investigated patient corticomotor response to treatment highlights the need for more research in this area. Our understanding of how corticomotor function may contribute to improvements in swallowing following stroke will be enhanced with such investigations.

Despite the lack of evidence of patient corticobulbar response to intervention, some studies have used MEP measures to describe the differences in corticomotor function between patient populations and healthy controls (Ertekin, et al., 2001b; Gallas, et al., 2007; Khedr, et al., 2008). These studies offer important advances in understanding changes in corticobulbar function in dysphagic patients. UES MEPs (Khedr, et al., 2008) and mylohyoid MEPs (Gallas, et al., 2007) induced from the affected hemisphere of dysphagic patients are of smaller amplitude (Gallas, et al., 2007; Khedr, et al., 2008) and longer latency (Khedr, et al., 2008) than those recorded from healthy controls. Of interest in these studies is the comparison of dysphagic stroke patients to not only control participants but also to non-dysphagic stroke patients. The finding that MEPs from the affected hemisphere in non-dysphagic patients were larger than the equivalent from dysphagic patients, and that they mimicked those seen in healthy controls (Gallas, et al., 2007; Khedr, et al., 2008), indicates that TMS quantifies activation of neural pathways pertinent to swallowing control. This is supported by comparison of UES MEPs between dysphagic patients, non-dysphagic patients, and healthy controls (Ertekin, et al., 2001b). This comparison found that while all participants had MEPs in response to peripheral vagal nerve stimulation, cortically evoked MEPs were absent in patients with a hyper-reflexive UES and clinical signs of pseudobulbar palsy (Ertekin, et al., 2001b).

MEPs are typically recorded at several time points following completion of treatment protocols to show the time frame in which cortical excitability is influenced. These time points are typically spaced 15–30 min apart over 2–3 hours (Doeltgen, et al., 2010a; Fraser, et al., 2002; Fraser, et al., 2003; Gow, et al., 2004b; Jefferson, et al., 2009a; Jefferson, et al., 2009b; Mistry, et al., 2006; Mistry, et al., 2007; Power, et al., 2004; Wahab, Jones, & Huckabee, 2010). This is an important component of MEP studies as it provides insight into differential effects of dose and frequency manipulations. Because adaptations to corticomotor

excitability following many dysphagia treatments appear transient in nature (Doeltgen, et al., 2010a; Fraser, et al., 2002; Fraser, et al., 2003; Gow, et al., 2004b; Mistry, et al., 2006; Mistry, et al., 2007; Wahab, et al., 2010), it is imperative to couple these neural changes with modifications in swallowing function. This is particularly important for studies that have documented inhibitory effects of treatments on the excitability of swallowing pathways (Fraser, et al., 2003; Jefferson, et al., 2009a; Jefferson, et al., 2009b; Mistry, et al., 2006; Mistry, et al., 2007). If it is shown that an increase in MEP amplitude and a decrease in MEP latency are related to positive functional response to treatment (and the reverse is related to a negative functional response), MEPs can provide evidence of treatment efficacy at the corticomotor level, with changes indicative of a possible mechanism responsible (or at least in part) for improvement or decline in swallowing function.

### ***3.1.1.3 The relationship between MEPs and swallowing function***

MEPs do not reflect swallowing biomechanical processes, and therefore do not provide a direct functional measure of swallowing *per se*. However, documenting modification of corticomotor function may provide insight into the underlying mechanisms behind altered biomechanics. To link changes in MEPs with swallowing function, some studies have concurrently quantified other swallowing measures after treatments. Temporal measures of swallowing such as swallowing reaction time (SRT) (Fraser, et al., 2002; Jefferson, et al., 2009a; Mistry, et al., 2007; Power, et al., 2004), oral transit time (OTT) (Power, et al., 2004), pharyngeal transit time (PTT) (Fraser, et al., 2002; Power, et al., 2004), UES opening duration (Power, et al., 2004), and laryngeal closure duration (Power, et al., 2004) have been used to monitor functional adaptations that occur in conjunction with MEP fluctuations. One research group has conducted a series of MEP studies using concurrent temporal outcomes which has rendered conflicting findings (Fraser, et al., 2002; Jefferson, et al., 2009a; Mistry, et al., 2007; Power, et al., 2004). A decrease in SRT was seen to coincide with a decrease in MEP amplitudes following inhibitory rTMS in healthy participants (Mistry, et al., 2007). The authors propose this was a maladaptive consequence, suggesting less control of the bolus and increased risk of aspiration with faster response times. This concept is supported by the finding that velocity of bolus propulsion through the pharynx is positively correlated with pharyngeal residue (Pauloski et al., 2009). A further study which found that decreases in MEP amplitudes coincided with decreases in SRT also found the reverse to be true (Jefferson, et al., 2009a). This study reports that decreased SRT and MEP amplitudes also coincided with

increased errors in a “challenged swallow” task (detailed in Mistry, et al., 2007, pp. 527-528), lending support to the conclusion that decreased MEP amplitudes may coincide with degraded swallowing function. Another study that documented decreased SRT did not find other swallowing behaviours were related to the concomitant decrease in MEP amplitude, including OTT, PTT, airway closure duration, and UES opening time (Power, et al., 2004). Furthermore, an increase in MEP amplitude seen by the same study was not related to any of the swallowing behaviour measures, including SRT. However, healthy participants were used which may explain why decreases but not increases in swallowing function could be induced. In contrast, a study by Fraser et al. (2002) found a decrease in swallowing response time was accompanied by no change in MEP amplitudes following pharyngeal electrical stimulation of dysphagic patients (Fraser, et al., 2002). Unfortunately the authors discuss a non-significant increase in MEPs as a true effect of the treatment. Rather than a maladaptive response, Fraser and colleagues attributed the decrease in SRT to enhanced swallowing function, as PTT and aspiration scores were also seen to decrease, and by their conclusions so did MEP amplitudes. Interestingly, while SRT but not MEP amplitudes changed in dysphagic patients the opposite was true for healthy participants in Fraser et al.’s study.

Other studies have documented increases in MEP amplitudes that do not reflect associated changes in pharyngeal pressures (Doeltgen, Heck, & Huckabee, 2010b; Wahab, et al., 2010). These studies proposed that while modifications of corticomotor function may result over a relatively short time frame following interventions, the effect of these changes on biomechanics is not immediately evident. This further confounds the picture of how fluctuations in MEP amplitudes may reflect adaptations of biomechanical characteristics of swallowing.

One issue with the discrepancies regarding temporal swallowing outcomes may be the method used to measure change. Indirect methods of SRT that rely on participants’ subjective responses (Jefferson, et al., 2009a; Mistry, et al., 2007) must be interpreted with caution. Using VFS to determine if influences on MEPs are reflected by changes in swallowing behaviours eliminates the subjective component of participant reaction to a cue but studies using this method have also rendered conflicting findings (Fraser, et al., 2002; Power, et al., 2004). This may be due to the subjective interpretation of VFS measures by the researcher. Furthermore, documenting change in temporal measures alone does not provide insight into



any changes in accuracy (Reis et al., 2008). The speed-accuracy trade-off could mean increased SRT, PTT, and OTT translates to a less efficient swallow (Jefferson, et al., 2009a; Mistry, et al., 2007; Pauloski, et al., 2009). However, the finding of decreased aspiration scores in conjunction with decreased temporal measures (Fraser, et al., 2002) indicates that this issue needs further investigation. Therefore, coupling changes in cortical excitability with changes in numerous measures of swallowing biomechanics would allow direct interpretation of the functional correlates between the two.

#### ***3.1.1.4 Reliability of MEP from swallowing muscles***

The reliability of submental MEPs (Al-Toubi, Abu-Hijleh, Huckabee, Macrae, & Doeltgen, 2010; Doeltgen, et al., 2009a; Gallas, et al., 2009; Plowman-Prine, et al., 2008), pharyngeal MEPs (Plowman-Prine, et al., 2008) and esophageal MEPs (Paine et al., 2006) have been assessed by a small number of studies. Of the four studies looking at submental MEPs, two have used intraclass correlation coefficients (ICCs) and two have used repeated-measures ANOVA, consequently comparison of results is limited to two studies in each group. When five trials were recorded at each session, the across-session reliability over two sessions was .78 (Plowman-Prine, et al., 2008), and decreased slightly to .66 across four sessions (Doeltgen, et al., 2009a). The study by Doeltgen et al. (2009a) found higher across-session reliability when 10 compared with 5 trials were used, with ICCs of .72, still slightly lower than those reported by Plowman-Prine (Plowman-Prine, et al., 2008) using 5 trials. Interestingly, Doeltgen et al. (2009a) found a decrease in across-session reliability when 15 trials were used in each recording block, with ICCs dropping to .69. However, with regards to within-session reliability, 15 trials elicited the highest ICC (.92), with the authors citing a reduction in ICCs with a reduction in MEP trials. This is supported by the finding that within-session reliability of esophageal MEPs improves over the first 10 trials, and declines with more than 15 stimuli (Paine, et al., 2006). While Plowman-Prine et al. (2008) claimed ICCs of .75 and over are high (Portney and Watkins, cited in Plowman-Prine 2008, pp 2301), Doeltgen et al. (2009a) used a more stringent classification of .90, with ICCs ranging between .70 – .80 as “good” (Atkinson and Nevill, 1998, cited in Doeltgen, et al., 2009a, p. 137). The two studies utilizing ANOVA revealed no differences in MEP amplitudes or latencies when no treatments were executed between recording blocks (Al-Toubi, et al., 2010; Gallas, et al., 2009).

Another issue with comparing results of studies investigating reliability of swallowing MEPs is the placement of electrodes. While most studies use surface electrodes for submental musculature, whether these are placed to measure activity of the right and left muscles separately (Plowman-Prine, et al., 2008), collectively (Doeltgen, et al., 2009a), or of one side only (Gallas, et al., 2009) varies from study to study. Therefore, reliability differences may be due to measurements being obtained from differential components of the submental muscle group.

Reliability of esophageal MEPs improves with higher stimulus intensities (Paine, et al., 2006). Higher stimulus intensities also heavily influence MEP size, the two increasing together (Paine, et al., 2006). Stimulus intensity is typically determined on an individual basis, influenced by motor threshold (Paine, et al., 2006), or MEP response size (Al-Toubi, et al., 2010; Doeltgen, et al., 2010a; Wahab, et al., 2010). Because of the variation in stimulus intensities applied, large variation is seen across participants and within participants when lower stimulus intensities are used, resulting in large standard deviations for group values (Wassermann, 2002). This variation is important to consider when investigating changes in the excitability of cortical projections (Paine, et al., 2006). While reliability studies have documented no significant changes in MEP measures across sessions (Gallas, et al., 2009), or moderate ICCs (Doeltgen, et al., 2009a; Plowman-Prine, et al., 2008), the variability reported in these studies indicates that relatively large group effects are required to override the inherent variability of swallowing MEPs. Studies frequently report standard deviations of around 50% of the mean (Al-Toubi, et al., 2010; Doeltgen, et al., 2009a) and as high as 140% (Plowman-Prine, et al., 2008). Supporting this proposition, a study of arm muscles found no difference in MEP amplitudes across three sessions (Wolf et al., 2004). However, coefficients of variation of amplitudes were relatively large (30-40%), suggesting this variability is substantial enough to mask any smaller differences across sessions. While variance estimates at the group level provide an idea of the size of effects required across-participants, within-participant variance estimates are not generally reported. Therefore, the magnitude of within-participant effects required to supersede change as a result of simply repeating the measure remains unknown.

### **3.1.1.5 *Factors affecting the amplitude of the MEP***

In addition to stimulus intensity, level of background muscle contraction also influences MEP amplitude (Darling, et al., 2006; Devanne, Lavoie, & Capaday, 1997). As MEP amplitude increases with magnitude of background muscle contraction, the variability of the MEP decreases (Darling, et al., 2006). Some level of muscle contraction also reportedly reduces MEP onset latency compared with MEPs taken from a resting muscle (Andersen, Rosler, & Lauritzen, 1999). As stimulus intensity and contraction levels have a cumulative effect on the amplitude (Darling, et al., 2006), a balance between facilitating the MEP amplitude to reduce variability and avoiding saturation needs to be achieved (Aranyi, Mathis, Hess, & Rosler, 1998). Furthermore, higher levels of contraction do not necessarily reduce variability over minimal levels of contraction (Darling, et al., 2006). However, these factors considered together indicate that MEPs taken from muscles during some level of contraction are less variable and allow lower TMS intensities to achieve quantifiable MEP amplitudes. As older participants require increased stimulus intensities to reach the same MEP amplitudes as younger counterparts (Pitcher, Ogston, & Miles, 2003), some level of contraction may facilitate recording cortical excitability in this population.

In further support of recording MEPs during muscle contraction, motor cortex excitability has been shown to increase during inactivity of the target muscles (Todd, Butler, Gandevia, & Taylor, 2006). Obtaining MEPs from muscles at rest requires participants maintain relaxed, inactive muscles for the duration of the investigation. It is proposed that a decrease in cortical inhibition associated with such restriction causes these fluctuations in motor cortex excitability (Todd, et al., 2006). However, one caution to consider when recording MEPs from a contracted muscle is that small fluctuations resulting from intervention may be masked (Andersen, et al., 1999). As small increases in background contraction have a large impact on amplitude (Darling, et al., 2006), pre-stimulus background EMG should be monitored to confirm consistent number of supra-threshold neurons across trials and tasks (Aranyi, et al., 1998). Studies have coupled the TMS discharge with a pre-set EMG trigger threshold in an attempt to maintain uniformity in the number of supra-threshold neurons (Al-Toubi, et al., 2010; Doeltgen, et al., 2010a; Wahab, et al., 2010).

The type of contraction performed at the time of cortical stimulation also has a bearing on the amplitude of the resulting MEP (Aranyi, et al., 1998). When triggering of TMS was kept at a

consistent EMG level between tasks, dynamic contractions (of increasing force) showed increased MEP amplitude compared with steady contractions (Aranyi, et al., 1998). The authors proposed that more neurons sit in a ‘ready’ state just below threshold in the dynamic condition, in anticipation of unexpected force requirements. This study found that changes in the length of the muscle during stimulation did not influence MEP amplitudes when EMG triggers were controlled (Aranyi, et al., 1998), suggesting that whether the goal of the movement was force or motion was irrelevant to fluctuations in cortical excitability. Specific to swallowing, significant differences in MEPs from the submental muscles have been documented across three tasks: volitional contraction, volitional swallowing, and reflexive swallowing (Doeltgen, et al., 2011). The authors reported a progressively larger MEP area from reflexive swallowing, to volitional swallowing, to volitional contraction, and proposed that this reflects increased M1 input for the contraction task over the brainstem-modulated tasks of swallowing. This assumption fits with the belief that the cortex plays a modulatory role in the primarily brainstem-generated swallowing response (Robbins, et al., 2008). A consideration of the comparison of these tasks is the use of area for quantification of the MEP size. While the authors controlled pre-stimulus activation of the target muscles across tasks using an EMG trigger system, the length of the volitional contraction was not controlled. As area of the MEP is influenced by both the magnitude and temporal characteristics of the EMG response, differences in the duration of muscle activation across tasks may result in a difference in MEP area unrelated to differences in cortical contribution.

While it has been shown that changes in the orientation of the coil, and therefore the flow of the underlying current, heavily influence MEP amplitude (Brasil-Neto et al., 1992; Kammer, Beck, Thielscher, Laubis-Herrmann, & Topka, 2001; Mills, Boniface, & Schubert, 1992), fixing the head and coil position has not shown any advantages over hand-held coil positioning (Ellaway, et al., 1998). Hand-held coil positioning involving stabilization of the coil against the head and scalp marking has been suggested to be sufficient to elicit reproducible MEPs (Al-Toubi, et al., 2010). While coil orientation affects amplitude, it has no impact on the variability of MEPs (Ellaway, et al., 1998), indicating that as long as coil angle is kept constant for repeated measures, no orientation is advantageous over others. However, for accessing greater amounts of underlying cortical projections to target muscles, a coil orientation of approximately 45 degrees towards the mid-sagittal plane on both hemispheres is recommended (Mills, et al., 1992).

An external influence on the quantification of MEPs is the filtering and analysis methods used. Various processes have been used to quantify MEPs, including averages from single-trial rectified EMG data (Doeltgen, et al., 2011; Ziemann et al., 1999), averages of single-trial unrectified EMG data (Doeltgen, et al., 2010a; Doeltgen, et al., 2009a; Gow, et al., 2004b; Jefferson, et al., 2009a; Mistry, et al., 2007), maximal MEP response (McDonnell, Ridding, & Miles, 2004), peak-to-peak amplitude and area of ensemble-average waveforms (Bastings, Greenberg, & Good, 2002; McDonnell, et al., 2004; Pitcher & Miles, 2002; Pitcher, et al., 2003), median value of single-trial unrectified data (Awiszus, 2005; Wolf, et al., 2004), and peak-to-peak values from an ensemble-median waveform (Awiszus, 2005). Quantifying MEPs based on area of rectified EMG data requires similar magnitude and duration of muscle contraction across tasks for MEPs recorded from pre-contracted muscles (mentioned above). Averaging of single-trial raw EMG has been shown to yield reliable results for submental MEPs from session to session during both swallowing (Doeltgen, et al., 2009a) and volitional contraction (Al-Toubi, et al., 2010) but details of how the initial peak is selected, and therefore how onset latency, as well as peak-to-peak amplitude is calculated, is generally not reported in the literature (Doeltgen, et al., 2010a; Jefferson, et al., 2009a; Mistry, et al., 2007). While studies frequently report filter settings of around 5 Hz – 2 kHz (Fraser, et al., 2003; Gow, et al., 2004a; Gow, et al., 2004b; Hamdy, et al., 1997; Hamdy, et al., 1998; Mistry, et al., 2006; Power, et al., 2004), increased filtering, including high pass filters of 100 - 200 Hz has also been reported (Mistry, et al., 2007; Oh, et al., 2007). Some studies report filters of “2 – 5 kHz” (Gallas, et al., 2007; Paine, et al., 2006; Verin & Leroi, 2009), which undoubtedly impact on the amplitude of the evoked potential. Some studies do not report filter settings utilized during data acquisition or analysis (Al-Toubi, et al., 2010; Doeltgen, et al., 2010; Jefferson, et al., 2009a; Jefferson, et al., 2009b). As filter settings often differ across studies, the effect of these settings on the size of the MEP must be considered when comparing results.

Even when the many factors influencing MEPs are controlled, large variability in amplitudes is still evident (Darling, et al., 2006; Ellaway, et al., 1998; Thickbroom, et al., 1999). Comparison of the variability of cortical MEPs to reflexes induced at the spinal neurons shows variation in the former is much larger than the latter (Kiers, et al., 1993), lending to the hypothesis that intrinsic fluctuations of cortical projections are largely responsible for the unexplained ‘noise’ (Darling, et al., 2006; Pitcher, et al., 2003). The unpredictable nature of

cortical excitability is highlighted by the finding that activation of facial muscles facilitates MEPs recorded from hand muscles (Andersen, et al., 1999). The authors propose that increased excitability of cortical areas that represent the face influence cortical areas in close proximity, such as the hand, and therefore serve to facilitate excitability of projections to both.

### **3.1.2 Limitations and future directions for measuring corticomotor function**

MEPs of swallowing muscles are sensitive to effects of various treatments. Studies to date have observed changes in cortical excitability over a relatively short period of time, typically over a duration of 2 – 3 hours. Rehabilitation programmes presumably aim to have a cumulative effect on corticomotor function to induce long-term changes in swallowing function in the case of neurogenic dysphagia. Long-term changes in cortical excitability of projections to swallowing muscles need to be documented to assess whether these adaptations are transient or more permanent in nature.

If cumulative effects are investigated using repeat sessions, parameters that affect MEPs must be controlled to ensure changes can be attributed to treatments rather than methodological error. The identified benefits of recording MEPs from contracted rather than resting muscles suggests that levels of activation at the time of stimulation need to be consistent across sessions. Coil orientation and hot spot location must also be kept constant across sessions, as well as stimulus intensity. Integration of the findings from studies investigating submental MEP reproducibility suggests 15 trials are required at each time point to ensure the maximum level of within- and across-session repeatability is achieved.

While MEPs recorded from swallowing muscles have been used to document changes in excitability of cortical projections, how these changes correlate to function remains uncertain. Future studies need to concurrently monitor changes in biomechanical and functional measures of swallowing if the mechanisms responsible for improved function following treatment techniques are to be understood.

Because of the large variability seen in responses within and across individuals, the size of response variability needs to be taken into account when assessing changes in the excitability of cortical projections (Paine, et al., 2006). Methods of analysis need to incorporate this

variance to ensure findings reflect true changes in the relatively noisy data sets that are inherent to MEP investigations.

As many steps in MEP analysis are not reported in the literature – for example, how the positive and negative peaks, or onset latency are determined – how these issues affect MEP quantification needs to be investigated to enhance comparison of results across studies. As MEP amplitude is reduced as filtering increases, with the amount of reduction dependent on what filter type and filter order is specified, investigations aiming to provide comparative data need to be explicit about filter settings. This information must also be considered when comparing across studies. When the level of filtering used imposes substantially on the MEP signal, how these values reflect true physiology must also be called into question.

## **3.2 Pressure in the pharynx**

### **3.2.1 Manometry**

Pharyngeal manometry is the only method of quantifying pressure in the pharynx during swallowing. It involves placing a catheter transnasally into the pharynx (Figure 3.3) and anchoring it in the UES. Catheters usually house three (Butler et al., 2009; Gumbley, Huckabee, Doeltgen, Witte, & Moran, 2008; Huckabee, Butler, Barclay, & Jit, 2005; Huckabee & Steele, 2006) or four (McConnel, Guffin, & Cerenko, 1991; Olsson, Nilsson, & Ekberg, 1995b) solid-state pressure sensors, allowing quantification of the degree and timing of pressure events in the oropharynx, hypopharynx, and UES during swallowing (Dodds, Kahrilas, Dent, & Hogan, 1987; Salassa, DeVault, & McConnel, 1998).



*Figure 3.3. Placement of the pharyngeal manometry catheter transnasally.*

Pharyngeal pressures have been evaluated in healthy participants to establish normative data for patterns and magnitude of pressure generation during swallowing (Castell & Castell, 1993; Olsson, et al., 1995b; Wilson, Pryde, Cecilia, Macintyre, & Heading, 1989). Criteria for defining disordered swallowing pressures have been attempted through manometric assessment of dysphagic patients (Desuter et al., 2009; Lazarus, Logemann, Song, Rademaker, & Kahrilas, 2002; Meier-Ewert et al., 2001; Olsson, Castell, Castell, & Ekberg, 1995a). The technique has also been used to document how healthy (Bulow, Olsson, & Ekberg, 1999; Huckabee, et al., 2005; Huckabee & Steele, 2006; McCulloch, Hoffman, & Ciucci, 2010; Poudoux & Kahrilas, 1995; Umeki et al., 2009; Witte, Huckabee, Doeltgen, Gumbley, & Robb, 2008) and dysphagic (Bulow, Olsson, & Ekberg, 2001; Lazarus, et al., 2002) pharyngeal pressures are influenced during execution of swallowing manoeuvres such as the effortful swallow (Bulow, et al., 1999, 2001; Huckabee, et al., 2005; Huckabee & Steele, 2006; Lazarus, et al., 2002; Poudoux & Kahrilas, 1995; Witte, et al., 2008), Mendelsohn manoeuvre (Lazarus, et al., 2002), supraglottic swallow (Bulow, et al., 1999, 2001; Lazarus, et al., 2002), tongue-hold manoeuvre (Doeltgen, Witte, Gumbley, & Huckabee, 2009b; Lazarus, et al., 2002; Umeki, et al., 2009), head-turn manoeuvre (McCulloch, et al., 2010; Takasaki, Umeki, Kumagami, & Takahashi, 2010), and chin-tuck manoeuvre (Bulow, et al., 1999, 2001; McCulloch, et al., 2010). The effect of bolus size on pharyngeal pressures has also been evaluated using this technique (Butler, et al., 2009; Gumbley, et al., 2008; Poudoux & Kahrilas, 1995).

One important consideration when interpreting results of studies using pharyngeal manometry is catheter assembly (Dodds, et al., 1987). Specifically, the diameter and shape of the catheter along with the position and the size of the sensors within the catheter all influence manometric signatures obtained during swallowing (Brasseur & Dodds, 1991; Dodds, et al., 1987; Lydon, Dodds, Hogan, & Arndorfer, 1975). Catheter size is largely determined by the type of sensor used: unidirectional or circumferential. Evidence of radial and longitudinal asymmetry in the pharynx and UES indicates that circumferential pressure sensors may be advantageous over unidirectional sensors (McConnel, et al., 1991; Sears, Castell, & Castell, 1991). Although circumferential sensors alleviate the issue of radial pressure asymmetry, the increased diameter required to accommodate the sensors may counteract this advantage when looking at pressures in the pharynx. Variation in manometric recordings has been confirmed in relation to an increase in catheter diameter (Lydon, et al., 1975; Olsson, et al., 1995b;



Wilson, et al., 1989) as well as in response to patient discomfort (Cook, Dent, & Collins, 1989a), which is amplified during procedures using a larger catheter. Bolus flow is also heavily influenced by catheter diameter (Brasseur & Dodds, 1991), suggesting a catheter of smaller diameter and, therefore, housing unidirectional sensors, may provide more representative pharyngeal pressures related to swallowing.

There is evidence indicating an advantage of an ovoid catheter in negating problems with recording asymmetric pressures (Castell & Castell, 1993; Salassa, et al., 1998). The ovoid shape assists with maintaining the sensors in a given direction (Castell & Castell, 1993; Salassa, et al., 1998), ensuring pressures are recorded from the same direction and presumably eliminating variance introduced by radial asymmetry. A study by Bardan et al. (2006) documented radial asymmetry in the UES when measures were made with a round catheter with four directional sensors but not when the same set up was incorporated in a flat sensor. They proposed that radial asymmetry arises from catheter assembly that is mismatched to the anatomy of the UES, rather than from physiological asymmetries. These findings suggest that asymmetrical readings can be eliminated by manipulating catheter shape. Alternatively, ensuring orientation stays constant throughout the recording can presumably prevent values being obtained from several directions.

### **3.2.1.1 *Manometry versus manofluorography***

Pharyngeal manometry can be paired with videofluoroscopy (manofluorography) to enhance interpretation of pressure waveforms. Manofluorography requires exposure to ionizing radiation, limiting accessibility of the technique. Exposing healthy participants to ionizing radiation is also ethically difficult to justify when attempting to obtain normative data. Manofluorography alleviates two issues that arise when using manometry in isolation: (1) uncertainty regarding the relationship between swallowing biomechanics and resulting manometric signals (Brasseur & Dodds, 1991) and (2) inability to objectively monitor sensor dislodgment during the swallow (Olsson, et al., 1995b). For accurate interpretation, the relationship between the manometric signal and the structures creating this signal must be understood (Brasseur & Dodds, 1991), strictly an impossible task without concurrent VFS. To assist with accurate interpretation of manometric signals in the absence of simultaneous VFS, some studies have documented the relationship between manometric recordings and swallowing biomechanics seen on videofluoroscopy (Cook et al., 1989b; Kahrilas & Shi,

1998; Olsson, et al., 1995b; Pauloski, et al., 2009). These studies provide some level of standardization and direction for interpreting manometry in isolation.

One study documented an artefactual spike of high pressure (around 600 mmHg) in the uppermost sensor associated with epiglottic flip, approximately level with the laryngeal inlet (Olsson, et al., 1995b). Another manometry signature known as the ‘M-wave’ (Castell & Castell, 1993) is created at the lowermost sensor during swallowing (Figure 3.4) and is used to assume placement at the proximal border of the high pressure zone of the cricopharyngeus muscle (Castell & Castell, 1993). The first peak of the ‘M’ is created by the sudden rise of pressure as hyolaryngeal excursion pulls the contracted UES onto the sensor. The drop in pressure forming the middle point of the ‘M’ reflects the negative pressure created by UES opening. As the UES returns to a state of tonic contraction, the final spike of the ‘M’ is created and finishes as hyolaryngeal excursion terminates and the UES is re-positioned below the sensor. The M-wave has been used to standardize catheter placement in numerous studies of pharyngeal pressures (Gumbley, et al., 2008; Huckabee, et al., 2005; Huckabee & Steele, 2006; Witte, et al., 2008). Location of the lowermost sensor at this position has been documented to most closely reflect UES measures made using videofluoroscopy (Kahrilas & Shi, 1998), and is necessary to record valid UES relaxation pressures during swallowing (Olsson, et al., 1995b). Further manofluorographic studies have documented that total swallowing duration measured with manometry is the same as that measured using VFS (Cook, et al., 1989b). A significant positive relationship has been documented between pressure recorded with manometry and duration of contact noted on VFS (Pauloski, et al., 2009). Furthermore, a negative correlation between pressure values and pharyngeal residue has also been documented (Pauloski, et al., 2009).

Two types of pressure related to swallowing can be measured using manometry: contact and intrabolus pressure. Contact pressure represents convergence of the pharyngeal walls or the functional peristaltic wave of the pharynx (Brasseur & Dodds, 1991). Intrabolus pressure, as the name suggests, is the pressure within the bolus, and is a more complex integration of factors (Brasseur & Dodds, 1991). Contact pressure is typically recorded rather than intrabolus pressure for several reasons. Firstly, intrabolus pressure cannot be recorded during saliva swallows, which are recommended in the assessment of pharyngeal pressures (Olsson, et al., 1995b). Secondly, interpreting intrabolus pressure is impossible without concurrent

VFS to identify location of the bolus around the sensor. Finally, intrabolus pressure fluctuates considerably relative to frictional forces, velocity and viscosity (Brasseur & Dodds, 1991; Olsson, Nilsson, & Ekberg, 1994) making it a complicated measure to obtain and interpret reliably (Olsson, et al., 1994, 1995b).

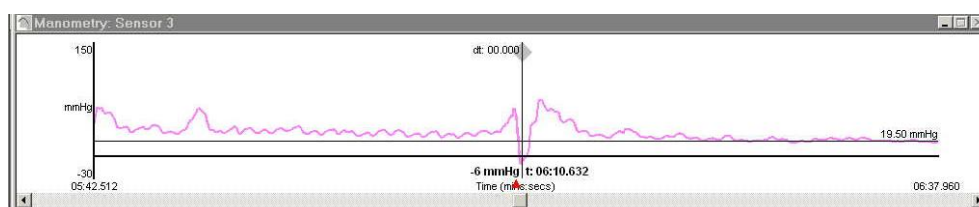


Figure 3.4<sup>8</sup>. Example of an M-wave at the lowermost sensor indicating placement in the proximal aspect of the UES. Note the elevated baseline which represents the tonic contraction of the cricopharyngeus muscle at rest.

Understanding the relationship between structures causing pressure events and the corresponding sensors is imperative if wanting to compare pharyngeal pressure values across participants. Sensor position is fixed in manometric catheters and placement (with or without VFS) is typically standardized using the M-wave in the lowermost sensor, consequently, the location of the upper sensors will vary slightly between people. This implies that even with direct visualization of the structures responsible for the signal in each individual (i.e., with manofluorography), comparisons of values across individuals is problematic due to differences in the location of oropharyngeal and hypopharyngeal sensors (Butler, et al., 2009). Furthermore, sensors approximate different structures at rest than during swallowing due to hyolaryngeal excursion and velopharyngeal closure (McConnel, et al., 1991), an issue that cannot be rectified with manofluorography. While manofluorography can assist with linking manometric signatures with an individual's anatomy, it does not address the issue that all sensors cannot approximate the same locations across individuals. Therefore, within-participant comparisons may be advantageous over across-participant comparisons, thereby ensuring differences in anatomy do not influence differences in pressure. Furthermore, the use of manofluorography may not be necessary to conduct within-participant evaluations if sensor position is kept stable through monitoring and maintaining catheter placement and orientation.

<sup>8</sup> Adapted from Daniels, S. K., & Huckabee, M. L. (Eds.). (2008). Chapter 13: *Dysphagia following stroke*. San Diego: Plural Publishing.

Asymmetric pressure recordings result when the catheter is dislodged during hyolaryngeal excursion and velopharyngeal closure (McConnel, et al., 1991). Manofluorography allows for monitoring and making adjustments to ensure sensor placement is consistent between swallows. If variance in manometric values is reduced by the use of concurrent radiography, studies using this method would presumably show reduced within-participant variation. Whether this is true remains unknown as studies typically report group means and standard deviations, meaning individual variance is lost. Similar means and standard deviations across the two methods may therefore be a result of across-participant variation. While average pressures in the hypopharynx reported for manofluorography are slightly larger (144 mmHg - Olsson, Kjellin, & Ekberg, 1996; 137 mmHg - Olsson, et al., 1995b) than reported for manometry in isolation (122 mmHg - Castell & Castell, 1993; 92 mmHg - Gumbley, et al., 2008), the standard deviations as a percentage of the means are similar for both at approximately 36% (Castell & Castell, 1993; Gumbley, et al., 2008; Olsson, et al., 1996; Olsson, et al., 1995b). The larger mean values documented by Olsson and colleagues (1996; 1995b) may relate to the larger diameter catheter used in these studies.

Whilst normative studies have used both manometry in isolation (Castell & Castell, 1993; Takasaki et al., 2008; Wilson, et al., 1989) and manofluorography (Olsson, et al., 1995b), large standard deviations are reported. This restricts comparison of disordered pharyngeal pressure values to normative values and hinders predictions about placement of sensors based on pressure readings in the absence of VFS. Furthermore, while some studies have reported significant differences in pharyngeal pressures when comparing regular saliva swallows with manoeuvre swallows (Doeltgen, et al., 2009b; Takasaki, et al., 2010), others have failed to find differences (Bulow, et al., 1999, 2001). It is crucial to reveal the cause of this variability if manometry is to provide a valid tool for documenting normative data and treatment outcomes. Deducing whether these large standard deviations are a result of within- or across-participant variation is a first step towards assessing the merits of manometry in conjunction with VFS versus manometry in isolation.

### **3.2.2 Limitations and future directions for measuring pharyngeal pressure**

Large standard deviations reported in manometry studies make it difficult not only to compare between studies but also to show treatment effects that are possibly smaller than the relatively

large variance. Cumulative effects of treatments on swallowing biomechanics may be especially sensitive to such masking. Studies using manometry in isolation or in conjunction with VFS need to document within-participant variability to assess whether variance is reduced using manofluorography. This information is necessary for determining and eliminating the sources of variance that may limit the use of manometry for obtaining normative data and documenting treatment outcomes. As no studies have used repeated manometry to document cumulative treatment effects on contact pressures, the variance reported in studies must be considered when interpreting results. Furthermore, studies employing manometry need to ensure stringent control of catheter orientation and placement to ensure the contribution of methodological error to the variance is minimized.

### **3.3 Muscle size**

The correlation between muscle fibre enlargement (hypertrophy) and an increase in muscle strength is well recognized (Esposito, Ce, Gobbo, Veicsteinas, & Orizio, 2005; Folland & Williams, 2007; Kanehisa et al., 2002; Rasch & Morehouse, 1957). This adaptation of muscle morphometry following exercise has been well documented in limb muscles (Jones, Rutherford, & Parker, 1989; McDonagh & Davies, 1984) but has scarcely been investigated for muscles innervated by cranial nerves, despite the fact that most dysphagia treatments aim to increase muscle strength (Burkhead, et al., 2007). The submental muscle group is the target of many swallowing rehabilitation techniques (Doeltgen, et al., 2010a; Shaker et al., 2002; Shaker, et al., 1997) and may consequently demonstrate hypertrophic change in response to strengthening exercise. However, given the functional, compositional, and neural control differences between muscles controlled by the spinal nerves and those controlled by cranial nerves (Chhabra & Sapienza, 2007; Kent, 2004), hypertrophic modification in these muscles requires further investigation.

Muscle morphometry has been assessed using a variety of imaging techniques, including MRI (Aagaard et al., 2001; Kubo et al., 2006; Narici, Landoni, & Minetti, 1992; Robbins, et al., 2005; Robbins, et al., 2007; Stonecipher, Jorizzo, Monu, Walker, & Sutej, 1994), computed tomography (CT) (Engstrom, Loeb, Reid, Forrest, & Avruch, 1991; Hudash, Albright, McAuley, Martin, & Fulton, 1985; Sipila & Suominen, 1993, 1995), and ultrasonography (Hodges & Gandevia, 2000; Maganaris, Baltzopoulos, & Sargeant, 2002; Reimers, Harder, & Saxe, 1998; Reimers, Schlotter, Eicke, & Witt, 1996; Scholten, Pillen, Verrips, & Zwarts,

2003; Sipila & Suominen, 1991, 1996; Stonecipher, et al., 1994; Watkin et al., 2001; Weiss, Clark, & Howard, 1988). There are several measures that can be taken from a muscle using any of these methods, including volume (3D), cross-sectional area (2D), and thickness (1D) (Figure 3.5).

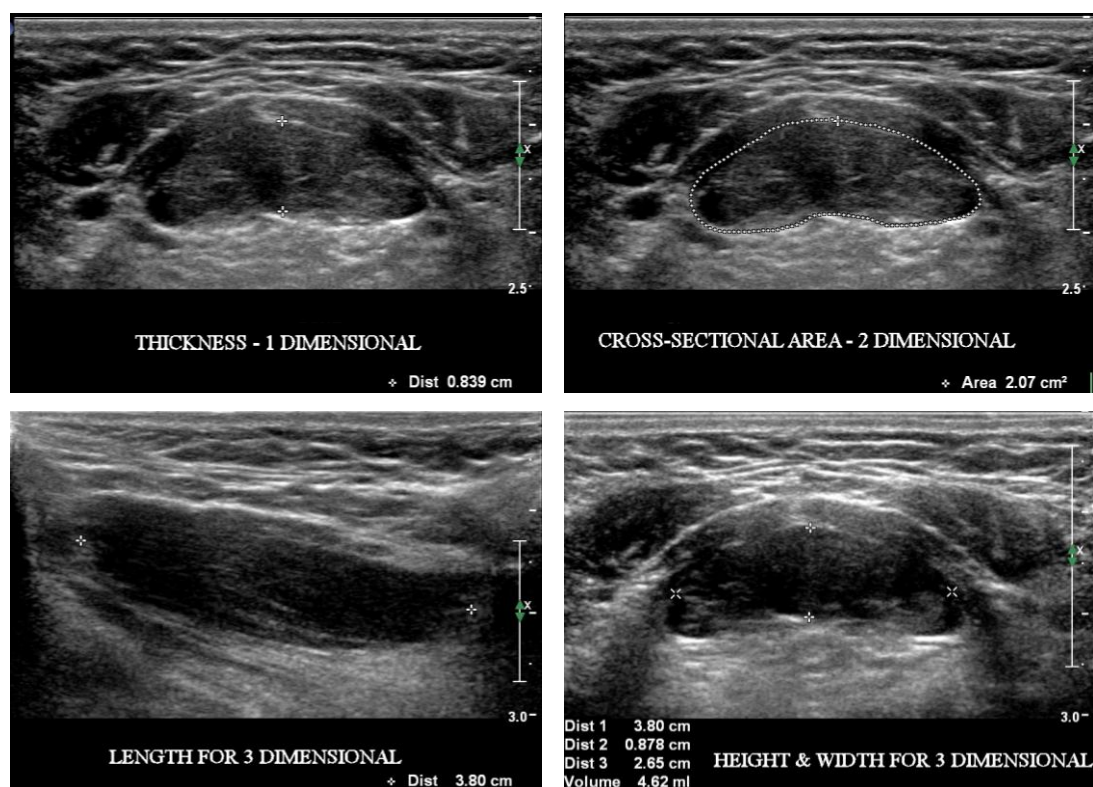


Figure 3.5. Examples of thickness (upper left), CSA (upper right), and volume (lower left and right combined) images for muscle measurement using ultrasound.

The complexity of data acquisition and processing is a consideration when weighing up whether to quantify muscle measures from 2D or 3D images. Data acquisition for 2D images is faster and less complex than 3D images in ultrasound but is the same for MRI and CT, where the distinction between planar and cubic measures is made off-line. Acquisition of 3D measures from ultrasound involves differential transducer placement, therefore introducing another variable into data acquisition. Calculating cross-sectional area (CSA) and muscle thickness is less involved than calculating volume regardless of which imaging method is used. CSA measurements have been reported to be more closely related to hypertrophy and force-producing characteristics than measures of thickness (Bemben, 2002). CSA has also been shown to be a reliable measure in leg muscles (Boonstra, van Weerden, te Strake, & Hillen, 1988; Juul-Kristensen, Bojsen-Moller, Holst, & Ekdahl, 2000a; Sipila & Suominen,

1995; Young, Hughes, Russell, Parkers, & Nichols, 1980) and head and neck muscles (Emshoff, Bertram, & Strobl, 1999). A study that documented the correlation between muscle volume obtained by MRI and muscle thickness obtained by ultrasound (Miyatani, Kanehisa, Ito, Kawakami, & Fukunaga, 2004) found the two measures to be significantly and highly correlated for arm and ankle muscles, and significantly but only moderately correlated for knee muscles. The authors concluded that muscle thickness, despite being acquired at a single location, “reflects its whole volume” (Miyatani, et al., 2004, p. 269). These results indicate that a 2D image may be a reliable proxy of muscle size and, therefore, a reliable measure of hypertrophic changes.

### **3.3.1 Magnetic resonance imaging (MRI) and Computed tomography (CT)**

MRI (Mitsiopoulos et al., 1998) and CT (Hudash, et al., 1985) have been validated in cadaver studies and are typically considered the “gold standard” (Bemben, 2002, p. 103) for assessing muscle morphometry, with MRI showing greater accuracy than CT (Engstrom, et al., 1991). The use of radiographic imaging when investigating muscle size in non-patient populations limits the application of CT, thus encouraging the use of techniques that rely on non-invasive methods, such as MRI. Furthermore, CT images do not distinguish between muscle and the surrounding thick connective tissue fasciae, leading examiners to include both in CSA measures (Sipila & Suominen, 1993). This results in decreased precision and inadequate definition between individual muscles (Hudash, et al., 1985) and a subsequent tendency for CT to overestimate muscle measures (Engstrom, et al., 1991).

MRI has been used to document hypertrophy in the CSA of neck muscles following exercise (Conley, Stone, Nimmons, & Dudley, 1997). Specific to swallowing musculature, hypertrophy has been shown using MRI of healthy (Robbins, et al., 2005) and post-stroke participants (Robbins, et al., 2007) following eight weeks of resistance training for the tongue. Training involved 10 presses of the tongue against a resistance device, three times per day on each of three days a week. These studies showed an average increase of approximately 5% in muscle bulk. Pharyngeal constrictor muscles also exhibit increased thickness following radiation therapy when imaged with MRI (Popovtzer, Cao, Feng, & Eisbruch, 2009). These results signify that enlargement is possible in the muscles of swallowing and that MRI is sensitive to such changes.

### 3.3.2 Ultrasound

Ultrasound has been used extensively to document various measures of limb muscle size (Hodges, Pengel, Herbert, & Gandevia, 2003; Maganaris, et al., 2002; Reimers, et al., 1998; Reimers, et al., 1996; Scholten, et al., 2003; Sipila & Suominen, 1991, 1996; Stonecipher, et al., 1994; Wallgren-Pettersson, Kivisaari, Jaaskelainen, Lamminen, & Holmberg, 1990; Weiss, et al., 1988). It is sensitive to both atrophic and hypertrophic changes in leg muscles (Reimers, et al., 1998; Reimers, et al., 1996), suggesting a place for this relatively inexpensive and non-invasive imaging method in detecting such changes in swallowing musculature.

Visualization of the submental muscles was first reported using coronal gray-scale ultrasound images by Shawker and colleagues (Shawker, Sonies, & Stone, 1984). However, very few investigations have utilized ultrasound to assess the morphometry of these muscles since this first publication. Increased CSA of the geniohyoid muscle (Figure 3.6) in patients following radiation therapy has been documented compared to healthy controls (Watkin, et al., 2001). While the mechanisms of enlargement following radiation exposure and neuromuscular exercise are distinct, this study indicates that ultrasound may be sensitive to detecting enlargement of these muscles. This study also assessed convergent validity by correlating ultrasound and histological measures from bovine samples (Watkin, et al., 2001). A study by Emshoff and colleagues (1999) found ultrasound to be a reliable method of measuring the anterior belly of the digastric muscle across two sessions, with a time lapse of more than 5 min between image acquisitions. This study used an average of three CSA measures from consecutive sections of the muscle belly.



*Figure 3.6<sup>9</sup>. Example of calculation of CSA of the geniohyoid muscle used to detect enlargement following radiation therapy.*

<sup>9</sup> Reprinted from Head Neck, 23(6), Watkin, K. L., Diouf, I., Gallagher, T. M., Logemann, J. A., Rademaker, A. W., & Ettema, S. L., Ultrasonic quantification of geniohyoid cross-sectional area and tissue composition: a preliminary study of age and radiation effects, 467-474, Copyright (2001), with permission from John Wiley and Sons.



Several studies have contrasted MRI and ultrasound images for limb muscle quantification. A study comparing the size of foot muscles obtained from the two methods was unable to compare the same muscles due to the inability to pre-select specific muscle portions prior to MRI scanning (Severinsen, Obel, Jakobsen, & Andersen, 2007). Some studies have reported lower spatial definition in ultrasound compared with MRI (Juul-Kristensen, et al., 2000a; Schedel et al., 1992) but the authors reported that these constraints are offset by the accessibility and lower cost of ultrasound. Furthermore, while MRI has excellent spatial definition, it is sensitive to motion artefact. High-resolution structural MRI is acquired over a longer duration (several min) compared with planar ultrasound images (1 s), making degradation due to movement artefact much more likely for MRI images. This trade-off in MRI is of little concern when investigating limb muscles that can remain in a relaxed state for relatively long periods of time. The issue becomes more of a concern when looking at the muscles of swallowing that are unavoidably activated approximately once every minute for swallowing saliva (Rudney, Ji, & Larson, 1995).

Differences in the signal generation of MRI and ultrasound might also warrant consideration for imaging the submental muscles. As MRI generates a signal based on proton density, muscles sitting in close proximity may not be clearly distinguished from one another. Ultrasound relies on the change in reflective properties from adjacent tissue to generate distinct boundaries. Therefore, in the confined space housing the submental muscles, images obtained from MRI may not provide the same level of surface detail required for precise muscle measurements. The positioning of participants is also a possible advantage of ultrasound. MRI requires participants to be supine for imaging, which may alter the swallowing musculature (Stemper et al., 2010). For ultrasound imaging, participants can be seated upright with the head in a neutral position.

Image quality control is another consideration when contemplating the best method of imaging the submental muscles. With MRI, images can only be processed off-line and, therefore, patient movement or re-positioning cannot be detected during image acquisition. Hence, re-acquisition in the case of artefactual data may prove inefficient and time-consuming. With ultrasound, image quality can be scrutinized on-line, allowing immediate acquisition of further images in the case of movement or unsatisfactory muscle borders.

### **3.3.3 Limitations and future directions for measuring muscle size**

The use of CT to detect changes in muscle size is limited by the use of ionizing radiation. While MRI eliminates this exposure, it presents a costly method of investigation for researchers. Ultrasound provides another method of investigating muscle size, eliminating many issues that surround the use of CT and MRI. Two-dimensional calculations made with ultrasound are less complex than 3D measures, and are reportedly reproducible for swallowing muscles (Emshoff, et al., 1999), and valid for limb muscles (Miyatani, et al., 2004).

There is a paucity of literature documenting changes in the morphometry of swallowing musculature. While the work by Emshoff and colleagues (1999) concludes images of submental musculature obtained from ultrasound are repeatable, comparison of ultrasonographic images against MRI would determine if image quality is compromised when utilizing the former, as reported for other muscles (Juul-Kristensen, et al., 2000a; Juul-Kristensen, Bojsen-Moller, Holst, & Ekdahl, 2000b; Schedel, et al., 1992). Further research is also required to assess the reliability of ultrasound measures in this muscle group obtained with a longer period of time between sessions. Additionally, validation of CSA measures from a single ultrasonographic ‘slice’ would simplify the process of documenting change in these muscles. If these issues are investigated further with satisfactory results, hypertrophy of the submental muscles following swallowing exercise can potentially be documented using ultrasound. This would decrease the cost and time of image acquisition and increase accessibility to instrumentation.

## **3.4 Hyoid displacement**

### **3.4.1 Videofluoroscopy**

Hyoid displacement is commonly investigated with videofluoroscopy (VFS) for both clinical and research purposes (Ford, Gollins, Hobson, & Vyas, 2009; Wheeler-Hegland, Rosenbek, & Sapienza, 2008). VFSS provides a dynamic radiographic video of the swallowing process, from sagittal and coronal views. The difference in contrast provided by the hyoid bone and surrounding tissue in the sagittal plane results in a relatively clear picture of hyoid displacement during swallowing. Quantifying the temporal relationship between hyoid

displacement and other biomechanical events is relatively straightforward, requiring only a time-code generator synchronized to the recording (Crary, et al., 2006).

Quantification of spatial aspects typically requires an involved process of calibration and data transformation (Humbert et al., 2006; Kendall, Leonard, & McKenzie, 2001; Kim, Han, & Kwon, 2010; Leonard, Kendall, McKenzie, Goncalves, & Walker, 2000; Logemann et al., 2000; Paik et al., 2008; Wheeler-Hegland, et al., 2008). Studies often utilize a reference marker against which measures of hyoid displacement are calibrated. This involves attaching a radiopaque marker to the participant (Gay, et al., 1994b; Humbert, et al., 2006; Kang et al., 2010; Kendall, et al., 2001; Kendall, McKenzie, Leonard, & Jones, 1998; Kim, et al., 2010; Leonard, et al., 2000; Logemann, et al., 2000; Paik, et al., 2008) or insertion of a pharyngeal manometer (Ford, et al., 2009; Kern et al., 1999) to ensure a known distance is recorded alongside the movement of interest. Images are then scaled to the reference marker to deduce accurate measures, unaffected by the distance of the participant to the x-ray source during acquisition (Figure 3.7). While this method ensures distance in the recorded 2D plane is accurate, it does not allow for control of neck flexion or lateral head movement away or towards the VFS source. While monitoring the distance of the radiopaque disc is considered sufficient to control such position changes (Logemann, et al., 2000), the circularity of discs produces the same constant distance irrespective of lateral and superior-inferior flexion. Therefore, the measured value may not accurately reflect hyoid displacement in the absence of positioning controls. Furthermore, if repeat measures are to be compared, differences in values as a result of changes in positioning cannot be ruled out.

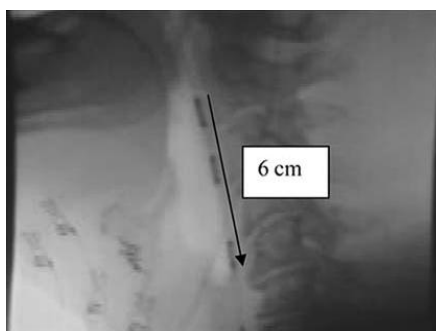


Figure 3.7<sup>10</sup>. A VFS image showing a pharyngeal manometric catheter in situ for calibrating distance of hyoid displacement.

<sup>10</sup> With permission from Springer Science+Business Media: Dysphagia, Structural displacements during the swallow in patients with early laryngeal cancers and other early primary cancers of the head and neck, 24(2), 2009, page 130, Ford, S., Gollins, S., Hobson, P., & Vyas, S., Figure 1.

To control for head movement when calculating displacement, some studies have measured hyoid trajectory relative to components of the vertebral column (Figure 3.8) (Humbert, et al., 2006; Kang, et al., 2010; Kim, et al., 2010; Leonard, et al., 2000; Logemann, et al., 2000; Paik, et al., 2008; Wheeler-Hegland, et al., 2008). While this controls for neck flexion to a certain degree, changes in the angle of the neck higher than the reference point (typically C2-C4) will not be detected. Furthermore, C1 (above C2) has the primary role in superior-inferior neck flexion and, along with C2, largely controls lateral flexion (Marieb, 1992), therefore movement in these planes may go undetected.

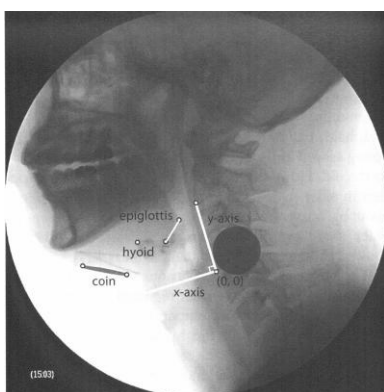


Figure 3.8<sup>11</sup>. Example of hyoid displacement analysis using a radiopaque marker and the anterior-inferior border of C4 and C2 as reference points for distance calibration.

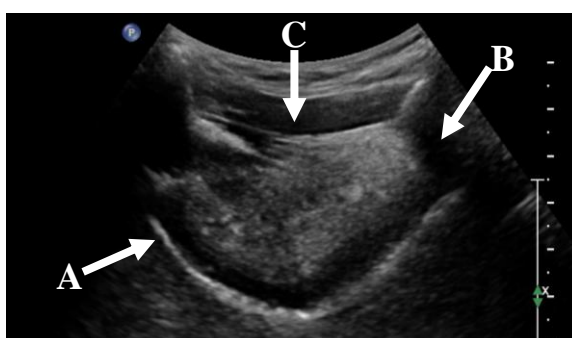
Studies using VFS to document hyoid displacement typically report standard deviations of approximately 30% (Ford, et al., 2009; Kendall, et al., 2001; Leonard, et al., 2000). While studies have documented adequate inter- and/or intra-rater reliability of measures made from the same images, i.e., ICCs greater than .80 (Humbert, et al., 2006; Kendall, et al., 1998; Leonard, et al., 2000), no studies have assessed reliability across repeated VFS studies. Therefore, the relative variance presented by methodological error and within- or across-participant variation cannot be determined. One likely reason for a lack of repeat studies using VFS is cumulative ionizing radiation exposure. Consequently, the use of videofluoroscopy to document normative data in healthy participants is difficult to justify (Cordaro & Sonies, 1993). Another disadvantage of using VFS for documenting hyoid displacement during swallowing is that ‘real’ food textures cannot be used, as the substance being swallowed must be mixed with a contrast agent such as barium.

<sup>11</sup> Reprinted from Gerontology, 56(5), Kang, B. S., Oh, B. M., Kim, I. S., Chung, S. G., Kim, S. J., & Han, T. R., Influence of aging on movement of the hyoid bone and epiglottis during normal swallowing: a motion analysis, 474-482, Copyright (2010), with permission from S. Karger AG, Basel.

The use of VFS for analysis of hyoid displacement requires complex processes of data calibration and transformation to alleviate methodological error. Additionally, the exposure to ionizing radiation limits normative data from being obtained, prompting utilization of other methods to quantify hyoid displacement.

### 3.4.2 Ultrasound

Ultrasound offers a relatively inexpensive and non-invasive method of investigating hyoid displacement. The method has received little attention in the literature, despite its documented use for acquiring temporal measures of oropharyngeal movements during swallowing over 2 decades ago (Sonies, Parent, Morrish, & Baum, 1988). Ultrasound utilizes a transducer that converts electrical energy into sound waves (Walker, Cartwright, Wiesler, & Caress, 2004). The soundwaves are converted back to electrical energy after being reflected back from the tissues of interest (Walker, et al., 2004). Tissues/structures are differentiated in the ultrasound image based on their reflective properties and distance from the transducer (Walker, et al., 2004). While the hyoid cannot be visualized directly with ultrasound (Chi-Fishman, 2005; Cordaro & Sonies, 1993), indirect measures of displacement can be made from visualizing the muscular attachments and the acoustic shadow of the hyoid bone. The acoustic shadow begins beyond the surface of the impenetrable hyoid bone and represents the disruption of ultrasound transmission (Figure 3.9). Real-time ultrasound provides a simple method by which to quantify temporal measures of hyoid displacement (Dejaeger & Pelemans, 1996; Ishida, Mukai, & Egusa, 2005; Sonies, et al., 1988). When quantifying spatial measures of hyoid displacement, studies utilizing ultrasound have historically required the same complex calibration and transformation processes as VFS (Chi-Fishman & Sonies, 2002a, 2002b).

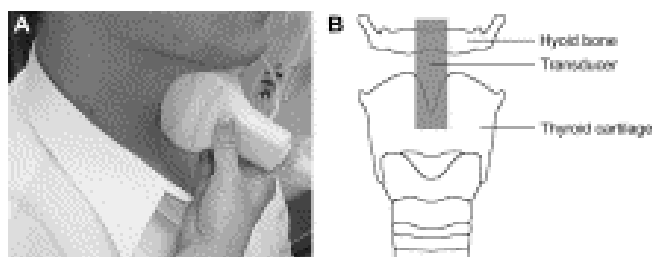


*Figure 3.9. Example of the acoustic shadow created by the hyoid bone. Image appears inverted, with transducer to skin contact at the superior edge of the image and anterior tongue surface (A) inferiorly.*

*The acoustic shadow (B) begins beyond the hyoid bone, with the sagittal view of the geniohyoid muscle (C) perpendicular to the acoustic shadow of the hyoid.*

Researchers using ultrasound to document thyroid elevation during swallowing have avoided complex data transformation and calibration (Huang, Hsieh, Chang, Chen, & Wang, 2009; Komori, Hyodo, & Gyo, 2008; Kuhl, Eicke, Dieterich, & Urban, 2003). Because of the small distance between the hyoid bone and the thyroid cartilage, a single ultrasound transducer can visualize the edges of both structures (Figure 3.10). Distances acquired during swallowing are therefore relative to a ‘rest’ position, rather than a single absolute value (Figure 3.11). The advantage of this method is that displacement can be expressed as a percent change from rest, eliminating the need for complex calibration and transformation. Expressing displacement as a percent change is crucial for across-participant comparisons (Chi-Fishman, 2005; Huang, et al., 2009). Using this method, calculations can be made on the ultrasound instrumentation, where calibration is intrinsically relative to the settings of the image acquisition. No studies to date have used this referencing system to measure the anterior displacement of the hyoid during swallowing, mainly because of a lack of reference for the hyoid due to the limited field of view of most transducers (Kuhl, et al., 2003).

The few studies that have utilized ultrasound to document hyoid displacement have required the same complex data transformation and calibration as studies using VFS. An alternative method of measurement could be to utilize a reference point for hyoid displacement, as done by researchers investigating thyroid elevation during swallowing (Huang, et al., 2009; Komori, et al., 2008; Kuhl, et al., 2003). This would allow non-invasive quantification of normative hyoid displacement with relative ease.



*Figure 3.10<sup>12</sup>. Example of transducer placement for visualizing approximation of thyroid cartilage and hyoid bone during swallowing. Images incorporate two points so that displacement is calculated as a percent change from rest.*

<sup>12</sup> Reprinted from *Ultrasound in Medicine & Biology*, 35(7), Huang, Y. L., Hsieh, S. F., Chang, Y. C., Chen, H. C., & Wang, T. G., *Ultrasonographic Evaluation of Hyoid–Larynx Approximation in Dysphagic Stroke Patients*, 1103-1108, Copyright (2009), with permission from Elsevier.

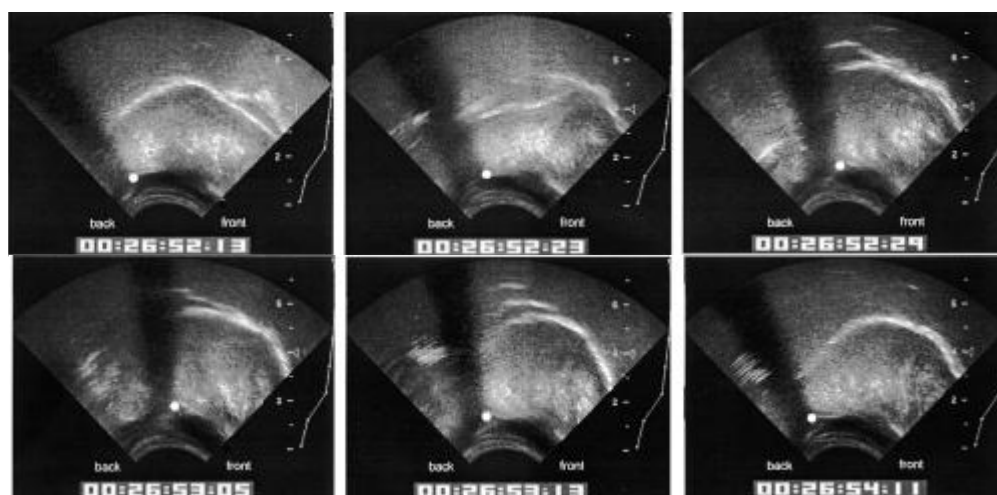


Figure 3.11<sup>13</sup>. Analysis of hyoid displacement (without a reference point). Distance travelled from the rest point is expressed as an absolute value. Data transformation and calibration is required to ensure distance measured on the image reflects true displacement values.

Like investigations using VFS, some ultrasound studies have calculated inter- and/or intra-rater reliability assessments on measures made from the same set of images (Chi-Fishman & Sonies, 2002a, 2002b). Also like VFS studies, the reliability of repeat ultrasound for assessing anterior hyoid displacement has not been assessed. However, the repeatability of ultrasound to calculate percent change measures of thyroid elevation is reportedly high within and across two investigators (ICCs greater than .95) (Huang, et al., 2009).

Maintaining the position of the transducer relative to the position of the head is crucial to control for movement artefact and to ensure accurate measures of true hyoid displacement are obtained (Chi-Fishman, 2005). Studies have employed head and neck stabilization by securing participants' heads to the head rest of a dental chair with a soft head-band (Chi-Fishman & Sonies, 2002a, 2002b). These same studies also secured the transducer with a manipulable assembly allowing movements in three dimensions (Chi-Fishman & Sonies, 2002a, 2002b) (Figure 3.12). Head movement can occur in many planes, and the efficacy of this simplistic head stabilization has yet to be confirmed through repeat measures. While more stringent methods are available for head and transducer stabilization (see Stone, 2005 for review), these units are often cumbersome and not portable, and have historically been utilized for analysis of tongue motion (Stone & Davis, 1995).

<sup>13</sup> Adapted from Journal of Speech, Language and Hearing Research, 45(3), Chi-Fishman, G., & Sonies, B. C. (2002). Kinematic strategies for hyoid movement in rapid sequential swallowing, 457-468.

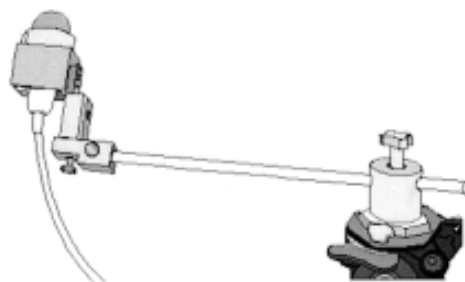


Figure 3.12<sup>14</sup> Transducer stabilization device allowing movement in three dimensions.

### 3.4.3 Limitations and future directions for measuring hyoid displacement

While videofluoroscopy provides a method to analyse both temporal and spatial characteristics of hyoid displacement, calibration and data transformation require reliability and precision assessments to determine their sensitivity to change. Furthermore, the required exposure to ionizing radiation limits normative and longitudinal data being obtained. Ultrasound offers a non-invasive and less expensive method of assessment. There are several factors that need to be considered and controlled when using ultrasound for spatial measures of hyoid displacement. Firstly, if repeated measures are to be comparable, the need for stringent methods of head and transducer positioning must be determined. As previous studies of hyoid displacement have not completed repeated sessions, the efficacy of their stabilization efforts cannot be determined. Given the axes on which head movements can occur, more rigorous methods may be required to ensure repeated measures reflect true values. Secondly, expressing calculations of hyoid displacement as a percent change from resting distance between the hyoid and a reference point would allow comparison of displacement across participants. The use of a transducer with a relatively large field of view would allow the use of the mental spine of the mandible as a reference for hyoid displacement. Due to the submental muscular attachments with the mental spine, this reference would be appropriate for measuring true anterior hyoid displacement during swallowing.

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<sup>14</sup> Adapted from Journal of Speech, Language and Hearing Research, 45(3), Chi-Fishman, G., & Sonies, B. C. (2002). Kinematic strategies for hyoid movement in rapid sequential swallowing, 457-468.



## **3.5 Muscle activation**

### **3.5.1 Electromyography (EMG)**

The most effective way of measuring muscle activation is with EMG (Perlman, et al., 1999), a technique of recording electrical muscle activity during exertion. EMG emerged as a diagnostic and research tool following the discovery that muscles generate electrical activity comprising superimposed motor unit action potentials (Ashley-Ross & Gillis, 2002). EMG is used for a variety of purposes, including quantification of the magnitude and temporal characteristics of muscle contraction (Ding, Larson, Logemann, & Rademaker, 2002; Huckabee, et al., 2005; Huckabee & Steele, 2006; Vaiman, Eviatar, & Segal, 2004a, 2004b; Yoshida, Groher, Crary, Mann, & Akagawa, 2007), detection of muscle abnormalities (Mills, 2005), and monitoring muscle fatigue (Dideriksen, Farina, & Enoka, 2010; Lind & Petrofsky, 1979; Myers & Lovelace, 1994; Shinohara & Sogaard, 2006).

Two commonly used methods of EMG in clinical and research environments are intramuscular and surface EMG. Intramuscular EMG uses needle electrodes inserted into the muscle(s) of interest (Mills, 2005), and is appropriate when recording activity from individual muscles contained in a small area (Palmer, Luschei, Jaffe, & McCulloch, 1999). Intramuscular EMG is typically used to define temporal patterns of muscle activation (Crary, et al., 2006). Surface electromyography (sEMG) uses electrodes placed on the skin surface overlying the muscles of interest (Crary & Groher, 2000), providing approximate values of the collective electrical activity of muscles in the vicinity of the electrodes (Palmer, et al., 1999). sEMG is often the method of choice in clinical environments, as it is non-invasive (Palmer et al., 2008) and provides a general picture of muscle activation during functional tasks (Crary & Groher, 2000). Specific to swallowing, the use of surface electrodes is often favoured for recording activation of the submental muscles, which are targeted by many EMG studies. In addition to the non-invasive nature of sEMG, it has been shown that when measuring from the submental muscles separately with needle electrodes, considerable within- and across-subject variability occurs in firing patterns (Cooper & Perlman, 1997; Spiro, et al., 1994).

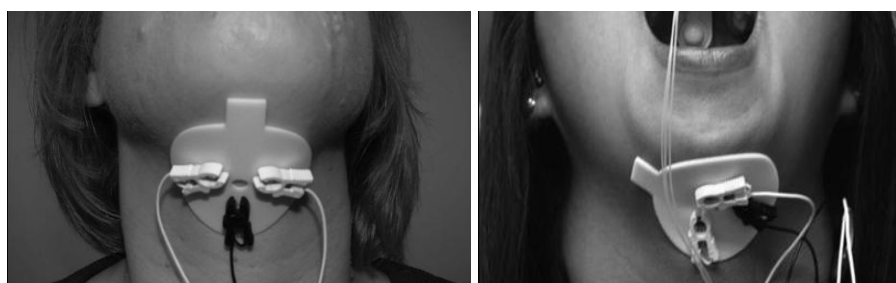
Investigations have used sEMG to explore the magnitude (Vaiman, et al., 2004b) and patterns of activation (Crary, 1995; Crary & Baldwin, 1997) during various swallowing conditions, and to describe the temporal relationship between muscles (Ding, et al., 2002). sEMG has also

been implemented as a form of biofeedback for dysphagia rehabilitation (Bryant, 1991; Crary, 1995; Crary, Carnaby Mann, Groher, & Helseth, 2004; Huckabee & Cannito, 1999). For accurate interpretation of sEMG it is crucial to know how the recorded signals relate to swallowing biomechanics (Crary, et al., 2006). The relationship between the signals and swallowing biomechanics is determined to some extent by electrode placement. Submental and infrahyoid (below the hyoid bone) electrode placements have been used to demonstrate muscle activity related to the pharyngeal phase of swallowing (Crary & Groher, 2000). While components of the oral phase of swallowing are detected with submental electrodes, this placement is recommended to record activity associated with the leading component of the pharyngeal swallow (Crary & Groher, 2000), and is more reliable than infrahyoid positioning when distinguishing between normal and manoeuvre swallows (Ding, et al., 2002). Submental electrode placement is also sensitive to changes in muscle activation related to varying bolus volumes and viscosities (Ertekin et al., 1997; Ertekin, et al., 1995).

The majority of studies evaluating changes in swallowing have utilized submental electrode placement, but the orientation of electrodes over these muscles differs between studies. While some studies have measured activity from the left and the right muscle pairs independently (Ding, et al., 2002; Palmer, et al., 1999; Vaiman, et al., 2004a, 2004b), others have used a single pair of bipolar electrodes to document activity from the midline of these muscles (Huckabee, et al., 2005; Huckabee & Steele, 2006; Lenius, Carnaby-Mann, & Crary, 2009; Wheeler-Hegland, et al., 2008; Yeates, Steele, & Pelletier, 2010). Furthermore, whether studies employ a single or double electrode pair, they also differ in the direction of recording. Some studies record between laterally oriented pairs (Figure 3.13) (Crary, et al., 2006; Wheeler-Hegland, et al., 2008), while others choose an anterior-to-posterior orientation (see Fig 3.13) (Huckabee, et al., 2005; Huckabee & Steele, 2006; Lenius, et al., 2009; Yeates, et al., 2010). These various placements presumably access the belly of the muscle, which is recommended in EMG recording as it detects the greatest amplitude (De Luca, 1997). Placement of one electrode pair in the midline has been validated using intramuscular EMG to show minimal contributions from muscles other than the submental muscles (Palmer, et al., 1999).

### **3.5.1.1    *The relationship between sEMG signals and swallowing biomechanics***

In an attempt to validate inferences of swallowing biomechanics from submental sEMG, a number of studies have assessed the association of submental sEMG with other swallowing measures. A close temporal relationship between both onset (Ertekin, et al., 2001a) and peak (Ertekin, et al., 1995; Sonies, Gottlieb, Solomon, Matthews, & Huckabee, 1997) submental sEMG activation and hyolaryngeal displacement has been documented, with the onset of the two events occurring within 10 ms (Ding, et al., 2002). The temporal relationship between these two measures is further reinforced by the finding that earlier onset of laryngeal and hyoid elevation during manoeuvre swallows coincides with earlier onset of submental muscle activation (Wheeler-Hegland, et al., 2008). However, translation of sEMG magnitude to spatial measures of hyoid displacement is not as straightforward as the temporal relationship. Greater sEMG measures at the point of maximum hyoid displacement coincided with greater hyoid displacement for only two of six comparisons (Wheeler-Hegland, et al., 2008), revealing that sEMG alone cannot determine the extent of hyolaryngeal displacement.



*Figure 3.13. Examples of sEMG submental electrode placement at midline: lateral orientation (left<sup>15</sup>) and anterior to posterior orientation (right<sup>16</sup>).*

Results from an early study reinforces the temporal relationship not only between hyolaryngeal excursion and submental sEMG, but also linked the two events to UES relaxation measured with intramuscular EMG (Ertekin, et al., 1995). This indirect relationship has been investigated in more recent studies showing submental sEMG measures were

<sup>15</sup> Adapted from Journal of Speech, Language and Hearing Research, 49(1), Crary, M. A., Carnaby Mann, G. D., & Groher, M. E. (2006). Biomechanical correlates of surface electromyography signals obtained during swallowing by healthy adults, 186-193.

<sup>16</sup> Reprinted from Journal of Oral Rehabilitation, 36(2), Lenius, K., Carnaby-Mann, G., & Crary, M. The relationship between lingual-palatal pressures and submental surface electromyographic signals, 118-123, Copyright (2009), with permission from John Wiley and Sons.

negatively correlated with UES pressures, measured with manometry (Huckabee, et al., 2005), and highly correlated with both hyoid elevation and UES opening, measured with VFS (Crary, et al., 2006). However, during effortful-swallowing, an increase in sEMG was significantly but only weakly correlated with a decrease in oropharyngeal and hypopharyngeal pressures (Huckabee, et al., 2005), implying the effect of sEMG magnitude on pharyngeal pressures may be too indirect to accurately interpret.

### **3.5.1.2 *Muscles contributing to the sEMG signal***

There is an ongoing debate in the literature regarding the contribution of other muscles to the submental sEMG signal. The finding that submental sEMG and tongue-to-palate pressure increase simultaneously has lead authors to propose that tongue muscle activation may also be being detected given the close proximity of submental and tongue musculature (Huckabee & Steele, 2006; Yeates, et al., 2010). Yoshida and colleagues (2007) found submental sEMG was greater during tongue-to-palate approximation than during the head-lift manoeuvre – a manoeuvre designed to activate the submental muscles – lending support for enhanced sEMG with tongue activation. However, the same study found only moderate correlations between tongue-to-palate pressures and sEMG. A further study found no significant correlation between these two measures, with consequent conclusions that while some lingual contamination of submental electrodes may occur, the sEMG signal in isolation is not enough to gain insight into lingual activation (Lenius, et al., 2009). The authors proposed that while the measures may fluctuate together, sEMG and tongue pressure measurements are most likely recorded from discrete muscles (Lenius, et al., 2009). In support of this conclusion, a study combining surface and intramuscular EMG has shown the largest contributions to the submental sEMG signal are from the mylohyoid, geniohyoid and anterior belly of digastric muscle, with minimal input from the genioglossus and platysma (Palmer, et al., 1999). A complementary study by the same authors (Palmer, et al., 2008) utilized intramuscular EMG in the same five muscles, while concurrently recording tongue-to-palate pressures. This study also found that increased tongue-to-palate pressures coincided with increased EMG of the submental muscles. Intramuscular recordings confirmed that while the two signals appear related, they are in fact distinct. Considered together, these findings indicate that contraction of the submental muscles increase when tongue-to-palate pressure increases, most likely to stabilize the floor of mouth to provide leverage for the tongue, but that submental sEMG is minimally contaminated by lingual activation.

### **3.5.1.3 *Factors affecting the amplitude of the sEMG signal***

EMG is often used to infer mechanical output of a muscle (Dideriksen, et al., 2010). Evidence that EMG amplitude is not correlated with functional strength or endurance estimates of leg muscles (Rodriguez & Agre, 1991; Rodriguez, Agre, & Shannon, 1988; Thorstensson, Karlsson, Viitasalo, Luhtanen, & Komi, 1976) suggests an indirect relationship between muscle strength and EMG (Cooper & Perlman, 1997). EMG amplitude is dependent on numerous factors, including the size of the electrodes, the size of muscle fibres, and the distance between the two (Myers & Lovelace, 1994). The relationship between amplitude and muscle force is also influenced by temperature (Myers & Lovelace, 1994) and fatigue of the target muscle (Dideriksen, et al., 2010; Lind & Petrofsky, 1979; Myers & Lovelace, 1994; Shinohara & Sogaard, 2006). A fatigued muscle requires greater activation levels to achieve the same amount of force as a non-fatigued muscle, resulting in a relative increase of EMG amplitude (Dideriksen, et al., 2010; Myers & Lovelace, 1994). A muscle in a state of fatigue can exhibit sEMG amplitudes of the same magnitude as a non-fatigued muscle that is exerting 40% more force (Dideriksen, et al., 2010). This increase is considered to be a result of synchronized firing, and the recruitment of additional motor units (Dideriksen, et al., 2010; Myers & Lovelace, 1994; Shinohara & Sogaard, 2006).

The length of a muscle also affects the ability of a muscle to generate force (Lindauer, Gay, & Rendell, 1993) and will therefore impact on EMG amplitude. While a linear relationship between sEMG amplitude and force measures of swallowing muscles has been demonstrated (Bakke, Michler, Han, & Moller, 1989), this linearity applies only when muscle contractions are isometric (Bakke, et al., 1989; Cooper & Perlman, 1997; Lindauer, et al., 1993). EMG characteristics from the muscles involved in jaw closure are only moderately correlated with force measures (Ottenhoff, vanderBilt, vanderGlas, Bosman, & Abbink, 1996), signifying that even the relatively slow and constant speed at which length changes for bite force (Ottenhoff, et al., 1996) is enough to disrupt this linear relationship (Lindauer, et al., 1993). The more rapid contraction rate of the submental muscles during hyoid excursion implies a similar non-linear relationship exists between sEMG and force for this event.

The number of other agonist or antagonist muscles contributing to a measured movement also influences the amplitude-force relationship of a given muscle (Ottenhoff, et al., 1996). The muscles chiefly responsible for hyoid displacement are in close proximity and, therefore, the

use of surface EMG is likely to provide a better illustration of the total magnitude of activation required for the event compared with movements in which contributing muscles are widespread. Surface EMG of these muscles is also likely to more accurately portray the total activation compared with single-muscle recordings from the same muscles made with intramuscular EMG.

Because of the complex relationship between EMG amplitudes and functional strength, some studies have proposed combinations of magnitude and temporal characteristics of EMG as a more reliable representation of mechanical output of a muscle (Ottenhoff, et al., 1996; Shinohara & Sogaard, 2006). Additionally, following the establishment of normative data, EMG patterns may prove useful in distinguishing abnormality for a particular movement (Walker, Hunt, & Williams, 1988). In the absence of normative pattern data, or complex methods of analysis, sEMG may provide a measure of muscle ‘excitability’, rather than a direct representation of mechanical output (Cooper & Perlman, 1997). Normative values for submental muscles report standard deviations of 33% (Vaiman, et al., 2004b), suggesting that changes in sEMG signals associated with swallowing need to be in excess of this to be detected. This large variation in values that are considered to be within the normal range is likely to be related to some of the factors that influence amplitude described above. As the distance between electrodes and the submental muscles will vary across people due to skin and subcutaneous tissue thickness, normative data may not provide a clinically useful tool without controlling these factors. As no studies have documented across-session variance of sEMG measures, these issues require further investigation. Furthermore, no studies have documented cumulative changes in activation of swallowing muscles associated with rehabilitation efforts.

### **3.5.2 Limitations and future directions for measuring muscle activation**

Midline submental sEMG recordings have been utilized extensively in investigations of swallowing biomechanics. While signals do not provide a direct measure of muscle strength, studies have correlated sEMG values with important biomechanical events during swallowing. By controlling as many variables as possible that affect the sEMG amplitude, submental recordings may provide a useful proxy for swallowing events, as demonstrated by previous researchers.

No studies to date have documented within- and across-participant variation in sEMG signals from swallowing muscles. This data is desirable for information on the effect sizes needed in treatment studies. Furthermore, the cumulative effects of treatments on sEMG parameters need to be documented to assess the usefulness of this technique in detecting changes in activation of swallowing musculature secondary to such treatments.

### **3.6 Requirements of measurement data**

There are many measures which assess the various components of swallowing. Determining the integrity and morphometry of the structures is possible with techniques such as MRI, ultrasound and VFSS. Movement of these structures can be documented during swallowing through the use of VFSS, ultrasound, and FEES. Functional swallowing pressures can be quantified using tongue pressure bulbs and pharyngeal manometry. It is also possible to document higher level functions such as cortical and corticomotor function using fMRI, EEG and TMS. Further outcome measures have also been constructed to quantify the psychosocial effects of dysphagia. As swallowing research is a relatively new area of focus, there are still many aspects of these measures that require verification. A review of the basic requirements of a measure is necessary when considering the strengths and weaknesses of methods available to the swallowing researcher.

There are three characteristics required for data obtained from a measure to be considered robust: they must be reliable, valid, and responsive (Roach, 2006). A definition of these terms is warranted to ensure clarity for the reader as these terms are used throughout the thesis. *Reliability* reflects the ability of a measure to produce consistent results when the same subjects are being measured under the same conditions (Field, 2005), indicating the degree to which the measure can be generalized across time points (Gatewood, Feild, & Barrick, 2008). Reliability is decreased by changes detected in the measure over time when no change is expected (de Klerk, 2008). These changes may be methodological or physiological in nature (Gatewood, et al., 2008). Reliability is typically expressed with a correlation coefficient calculated between two values which are obtained using the same measure from the same participants at two different time points, therefore representing a “coefficient of stability” (Gatewood, et al., 2008, p. 119). *Precision* estimates extend reliability assessments by quantifying the amount of variance associated with repeated-measures, incorporating both methodological and physiological change. Measurement precision is defined as the closeness

of agreement between values obtained from repeated measures on the same subjects under specified conditions (Joint Committee on Guides for Metrology, 2008). In contrast to reliability coefficients, precision is usually expressed by measures of imprecision, such as standard deviations calculated under the specified conditions of measurement (Joint Committee on Guides for Metrology, 2008). Precision is distinct from *accuracy*, which reflects the ability of a measure to quantify the true value. Precision simply reflects the ability of the measure to get the same value across repeated measures, whether accurate or not. While reliability provides a coefficient of stability, it does not translate to a specific amount of change expected from repeated-measures. The benefit of precision estimates is that they provide insight into the sensitivity of a measure and guide the establishment of desired effect sizes. For example, an effect that is substantially smaller than the precision estimates may have little clinical relevance given the magnitude is much less than that generated from simply repeating the measure. *Validity* assessments aim to ensure the accuracy of a measure, i.e., that it measures the phenomenon of interest (Roach, 2006). *Responsiveness* is defined as the ability of a measure to gauge clinical change (Wright & Young, 1997). Responsiveness assessments are required to ensure that measures are capable of detecting change considered clinically significant, therefore providing a useful measure in documenting functional change. Responsiveness assessments require knowledge of the magnitude of change considered clinically relevant and, therefore, rely on precision estimates, to specify the amount of change expected in the absence of treatment.

Reliability is important if decisions regarding patient management are to be based on the results of a measure, as there must be confidence that any changes are due to intervention rather than unrelated factors. As many measures used in swallowing research are performance based, assessments of intra- and inter-rater reliability are required. Because of factors such as rater- and participant-variance, the assumption that measures will remain stable across time in the absence of intervention is rarely valid (Roach, 2006). This is why reliability measures are applicable only for the specific purpose, population, and situation in which they are assessed (Dijkers et al., 2002). To alleviate the variance introduced by changes in participant response, assessments of intra- and inter-rater reliability can be performed on the same measures to ensure that reliability of rater performance is isolated.



Reliability is crucial to ensure consistent measures but is only useful if measuring the desired outcome. Like reliability, validity is not inherent in the measure but is dependent on the purpose, population, and circumstance of the assessment (Dijkers, et al., 2002; Roach, 2006). The most practical and objective form of validity assessment is criterion validity (Portney & Watkins, 2009). In this case, a ‘gold standard’ measure or criterion test is used to evaluate the results of the measure being validated (Roach, 2006). A limitation of criterion validity assessments is that the requirements of a ‘gold standard’ comparison include reliability and validity and, therefore, are rare in any area of clinical research (Portney & Watkins, 2009; Roach, 2006). A lack of gold-standard measures hinders the improvement of current tools and the development of alternative tools.

Some measures utilized in swallowing research do not directly reflect swallowing function and, therefore, validity assessments are not feasible or appropriate. A modification of validity assessment may be warranted in these situations. MEPs recorded from swallowing muscles reflect the function of the corticomotor pathways, rather than any specific biomechanical process. Additionally, sEMG and pharyngeal manometry provide insight into muscle activation, but not the ensuing events resulting from changes in that muscle activation. Utilizing these indirect measures is of interest as they may provide insight into a mechanism by which biomechanical processes or swallowing functions may be modified. However, to make clinical inferences from studies documenting changes in these measures, determining the clinical correlates of such modifications is required. Investigation of simultaneous changes in swallowing biomechanics may also assist with determining the magnitude of change in these indirect measures that could be classed as clinically relevant. While not considered validity assessment as such, relating changes in these measures with changes in swallowing function would assist researchers with determining the clinical relevance of alterations, and the responsiveness of these indirect measures to various treatments.

Responsiveness is usually quantified by effect sizes (Beaton, Bombardier, Katz, & Wright, 2001). Beaton et al. (2001) relate effect sizes to *p*-values, in that when they are considered in isolation they lack the context necessary for interpreting the meaning of such values. They therefore proposed a taxonomy of responsiveness, where the context in which the treatment effect was documented is considered. This idea proposes that, like reliability and validity, the relevance of clinical change depends on who is being studied and for what purpose. An

expectation of increased responsiveness from a measure in patients compared with healthy participants highlights the need for context specific measures of responsiveness. There is a scarcity of information regarding the responsiveness of swallowing measures for various populations. Estimates of responsiveness in any form, whether effect sizes or absolute difference, are necessary to aid researchers and clinicians in selecting appropriate measures. Additionally, studies that have assessed the responsiveness of measures have often investigated immediate adaptations associated with treatments, with very few assessing responsiveness to cumulative effects. In addition to estimates of variance, these measures are needed to facilitate calculation of statistical power in studies aimed at determining clinically relevant effects of treatment. Selection of appropriate measures in the absence of estimates of responsiveness and precision is based on assumption rather than logical analysis.

Precision estimates are crucial in the process of determining the responsiveness of a measure by providing researchers with insight into the magnitude of change expected inherent in simply repeating a measure, and therefore the amount of change required to exceed this variance. By defining the variance at different levels of the measure, such as within and across participants, precision estimates can be gained. Therefore, using estimates of within-participant variance provides the actual amount of change expected with repeating the measure in the absence of intervention. It also allows researchers to accurately propose participant sample size when aiming to reveal a desired effect. The process of selecting a desired effect however requires some knowledge of what magnitude of change is considered clinically relevant or significant. An effect size that is much smaller than the expected change from repetition of the measure alone may be revealed if sufficient participant samples are used, however, the clinical relevance of an effect of this magnitude may be questionable. Therefore measures need to be responsive to effects that are considered clinically relevant, requiring research that documents the functional significance of various effect sizes, which are presumably larger than the variance at a minimum.

While many measures have been utilized in swallowing research to document treatment outcomes, very few of these have undergone these fundamental assessments. While tests of reliability, precision, responsiveness, and validity seem like a relatively simple undertaking, one only has to consider the multitude of possible patient populations, the numerous applications of many measures (for example VFS), combined with the subjective variables

introduced by rater and context, to understand why these limitations continue to exist. Swallowing research is not unique in its limited assessment of measures. A study reviewing 1039 peer-reviewed publications from six US medical journals found validity was addressed for only 7% of measures, and reliability for 20% (Dijkers, et al., 2002). As reliability and validity are considered population specific, the authors further categorized studies into those that cited reliability and validity from other sources and those who provided “local evidence” (Dijkers, et al., 2002, p. 822). Context-specific reliability was provided in only 5% of all measures, with less than 1% of measures having context-specific validity. These issues need further attention if outcomes of swallowing research are to direct dysphagia management, or enhance our understanding of changes in swallowing. Reliability measures are required to gain insight into the stability of the assessment over repeated-measures. Precision estimates are required to determine the amount of change expected in the absence of treatment, therefore assisting with determining the sensitivity of measures, and establishing adequate participant samples for research studies. Responsiveness assessments are required to ensure measures are sensitive to effects of a magnitude considered clinically significant. Validity assessments of outcomes directly measuring swallowing function, or investigating the functional correlates of indirect measures ensures results of research studies are accurately applied to relevant swallowing processes.



## **Chapter 4: Objectives for methodological studies**

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### **4.1 Objective 1**

#### **Research question**

Investigations of hyoid displacement using ultrasound typically involve complex data transformation and calibration to ensure true values are recorded. Ultrasound studies expressing approximation of the thyroid cartilage and hyoid bone as a percent change rather than absolute values have been able to avoid such calibration and transformation issues due to the use of an anatomical reference point. The application of a reference point for calculating hyoid displacement has not been investigated.

#### **Objective**

To assess the application of the mentalis of the mandible as a reference point by which to quantify anterior hyoid displacement using ultrasound.

#### **Significance**

The reliable use of an anatomical reference point will allow expression of displacement as a percentage of rest measures, therefore eliminating the need for data calibration and transformation. This will enhance the opportunity for more widespread use of ultrasound to quantify hyoid displacement, and simplify research methods utilizing this measure.

#### **Proposed study (see Chapter 5)**

The intra- and inter-rater agreement of 'rest' and 'maximal displacement' measures between the hyoid and mentalis of the mandible will be assessed across three raters. Ultrasound video segments will record five swallows from each of five participants. One rater will assess each video segment twice for intra-rater reliability.

### **4.2 Objective 2**

#### **Research question**

MRI presents an expensive method of quantifying the size of the swallowing musculature. Additionally, the differences between limb and swallowing muscles may negate the

advantages of MRI reported by studies of limb muscles. No studies have compared submental muscle CSA measures made from ultrasonographic and MRI images to determine if image quality is compromised when utilizing the former, as reported for limb muscles.

### **Objective**

To assess the accuracy and utility of ultrasound as a method of quantifying CSA of the submental muscles relative to MRI.

### **Significance**

By assessing the capability of ultrasound to demarcate the submental muscles, the validity of this method in documenting CSA of the submental muscles can be determined. If ultrasound can provide this information, changes in oral musculature that result from factors such as exercise and atrophy secondary to disease or aging can be investigated with reduced cost and time compared with MRI.

### **Proposed study (see Chapter 6)**

CSA measures of the submental muscles will be taken from coronal ultrasound and MRI images in 11 healthy participants. CSA measures, strengths, and limitations of the two techniques will be compared to assess the optimal method of quantification for the submental muscles.

## **4.3 Objective 3**

### **Research question**

Various methods are reported in the literature for quantifying MEPs from swallowing muscles. Furthermore, details of the data analysis process are typically not provided by studies. The effect of utilizing different analysis methods on MEP outcomes is unknown.

### **Objective**

To compare various methods of MEP analysis to assess reliability of each, and the relationship between methods across five recording blocks with no treatment in between.

### **Significance**

As various methods are reported in the swallowing literature, the differential effects of these methods need to be elucidated for consideration when comparing results across studies. Documenting the reliability and the precision of these methods will enhance the knowledge of the sensitivity of MEPs to treatment effects.

### **Proposed study (see Chapter 7)**

An existing data set collected from 6 participants will be utilized to determine the reliability of various extraction methods. Five blocks of 15 MEPs were recorded from each participant and will be used in this analysis. Methods of analysis will include utilizing the mean value obtained from 15 individual trials, the median value from 15 individual trials, the ensemble-average waveform of the 15 trials, the ensemble-median waveform, and values from the rectified and averaged waveform.

## **4.4 Objective 4**

### **Research question**

No reliability assessments exist for repeat measures of pharyngeal manometry. Treatment studies utilizing this measure require assurance of reliable measures across assessment sessions to attribute changes to treatment.

### **Objective**

To document the within-participant variation in pharyngeal pressures both within and across three sessions.

### **Significance**

Direction for longitudinal treatment studies can be offered by providing a basis for power calculations, estimating values of any confounding order effects, and providing variance estimates.

### **Proposed study (see Chapter 8)**

Twenty healthy participants will be recruited for three sessions. For each session, peak or nadir pressures will be recorded from the oropharynx, hypopharynx, and UES during saliva and 10 mL water bolus swallows.





## Chapter 5: Intra- and inter-rater reliability for analysis of hyoid displacement captured by ultrasound<sup>17</sup>

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### 5.1 Introduction

Anterior hyoid displacement is essential for effective swallowing. Assessment of this biomechanical event is therefore of interest in both clinical and research environments. This movement of the hyoid is a component of hyolaryngeal excursion, a biomechanical event that lifts the larynx and hyoid bone in both a superior and anterior direction (Perlman & Christensen, 1997). This displacement is caused, in large part, by contraction of the submental (floor of mouth) muscles during swallowing, specifically the paired mylohyoid, anterior belly of digastric, and geniohyoid muscles. The results of this movement are two-fold: the epiglottis deflects to assist airway protection (Vandaele, et al., 1995) and the upper esophageal sphincter (UES) is pulled open to allow bolus transfer from the pharynx to the esophagus (Perlman & Christensen, 1997). Swallowing impairment (also known as dysphagia) is often characterized by reduced hyoid displacement during swallowing. Reduced hyoid movement has been associated with increased risk of airway invasion and pharyngeal residue (Steele et al., 2011), highlighting the need for accurate assessment of this biomechanical event in dysphagia management.

Hyoid displacement is commonly investigated with videofluoroscopy (VFS) (Kendall, et al., 2001; Kendall, et al., 2000; Wheeler-Hegland, et al., 2008). VFS provides visualization of temporal and spatial aspects of displacement; however, quantification of spatial aspects requires an involved process of calibration and data transformation (Kendall, et al., 2001; Leonard, et al., 2000; Wheeler-Hegland, et al., 2008). Additionally, the use of VFS to obtain normative data of hyoid displacement in healthy participants is difficult to justify due to cumulative ionizing radiation exposure.

Ultrasound offers a relatively inexpensive and non-invasive method of investigation but has received little attention in the literature, despite its documented use for acquiring temporal

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<sup>17</sup> **Macrae, P.**, Doeltgen, S., Jones, R., & Huckabee, M-L. (in press). Intra- and inter-rater reliability for analysis of hyoid displacement captured by ultrasound. *Journal of Clinical Ultrasound*.

measures of oropharyngeal movements during swallowing over two decades ago (Sonies, et al., 1988). Real-time ultrasound provides a simple method by which to quantify temporal measures of hyoid displacement. However, studies utilizing ultrasound have historically required the same complex calibration and transformation processes as VFS (Chi-Fishman & Sonies, 2002a, 2002b). A study by Scarborough and colleagues (2010) quantified hyoid trajectory in children without such data transformation or calibration. However, unlike previous studies, they did not employ stringent methods of head and transducer position control. Maintaining the position of the transducer relative to the head is crucial to control for movement artefact and to ensure accurate measures of true hyoid displacement are obtained (Chi-Fishman, 2005). As the method of calculating displacement in Scarborough et al.'s study cannot distinguish subtle transducer movement from genuine hyoid displacement, improved methods are required to control for the possibility of movement artefact. By restricting head and transducer placement, high reliability of hyoid measurement can be achieved (Chi-Fishman & Sonies, 2002a, 2002b). However, the use of head and transducer stabilization makes implementation of ultrasound in the clinical setting less straightforward, as units are often cumbersome and not portable (see Stone, 2005 for review). While simpler methods of head stabilization have been reported in studies of hyoid displacement (Chi-Fishman & Sonies, 2002b; Scarborough, et al., 2010), head movement can occur in many planes, and the efficacy of these simplistic methods is yet to be confirmed through repeat measures. The present study utilized ultrasound to quantify hyoid movement according to an anatomical reference point, therefore eliminating the need for data calibration and transformation, and providing a constant reference by which to monitor transducer movement. This preliminary study was conducted to assess the viability of this novel method through an evaluation of inter- and intra-rater reliability.

## **5.2 Method**

### **5.2.1 Participants**

Five healthy volunteers (2 males and 3 females, aged between 20-50 years) were recruited for one session. Participants had no history of surgery or disease affecting the head and neck musculature. Ethical approval was obtained from the local institutional review board. Informed consent was obtained prior to commencement of data collection.

### **5.2.2 Procedure**

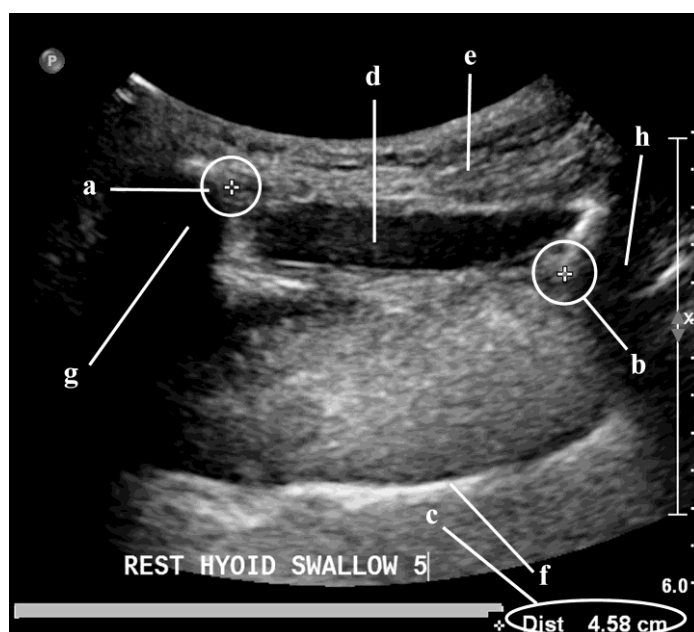
A Philips (Philips Healthcare, Surrey, UK) IU22 model ultrasonography unit was used with a 5-1 MHz curved array transducer. The C 5-1 MHz transducer provided a balance between adequate resolution and sufficient field of view to incorporate both the hyoid and the mental spine of the mandible bone in a single sonogram. Mid-sagittal grayscale sonograms were obtained as individual video segments of 8 s to record each swallow. Sonograms included the shadows cast by the hyoid and mental spine of the mandible. A generous amount of Aquagel™ was used for acoustic coupling and minimal pressure was placed on the floor of the mouth surface throughout sonogram acquisition so as not to distort swallowing movements. Sonograms were acquired and then processed offline.

The primary investigator acquired all sonograms. These were taken with the participant sitting upright. Participants were instructed to sit comfortably and relax their head in a neutral position. Once they had achieved this posture they were asked to maintain it while the transducer was placed under the chin, and not to accommodate the transducer with flexion of the neck. The transducer was placed in a sagittal plane, at approximately midline between the lateral edges of the mandible, perpendicular to the floor of mouth muscle group. Depth settings were tailored to accommodate individual anatomy, and gain settings were adjusted to allow optimal visualization of the shadows cast the hyoid and mental spine of the mandible. The participant was asked to maintain their tongue in a relaxed position when they were not swallowing. Once the researcher initiated recording of the video loop the participant was prompted to swallow their saliva as they usually would. Five swallows were recorded from each of the five participants. There was a time lapse of no less than 30 s between swallows so that participants could accrue saliva to avoid excess tongue movement prior to the subsequent swallow. The primary and two co-investigators completed data analysis to derive inter-rater reliability, with the primary investigator analysing the data a second time for intra-rater reliability.

### **5.2.3 Data analysis**

The five swallows of each participant were measured by the primary investigator, then independently by the other two investigators, followed by the primary investigator again. Each investigator was blinded to the measurements made by the other two investigators. As all swallow video segments were recorded by the primary investigator, reliability reflects

measurement of data only and not image selection. All measures were done in one session on the same day. Prior to data analysis, consensus was reached for definition of placement of the reference and hyoid displacement calipers as follows: the reference caliper was defined as the point at which the shadow created by the spine of the mandible intersected with the brightly echogenic cortical surface of the mandibular bone (see a in Figure 5.1 and 5.2); the hyoid displacement caliper was defined as the point at which the shadow created by the hyoid intersected with the geniohyoid muscle (see b in Figure 5.1 and 5.2).



*Figure 5.1. Sonogram of the hyoid/spine of mandible distance at rest. Electronic calipers mark the points at which the distance between mental spine of mandible shadow (a) and the intersection of the hyoid shadow with the geniohyoid muscle (b) is calculated (distance displayed at bottom right of sonogram (c)). Geniohyoid (d), skin surface (e), tongue surface (f), shadow cast by the mental spine of mandible (g), shadow cast by the hyoid bone (h).*

Each rater identified a ‘rest’ frame prior to any oral movement related to the swallow of interest and a ‘maximal displacement’ frame, at which the hyoid bone was at maximal anterior displacement during each swallow. Electronic calipers were used to measure the distance between the reference point and the maximal hyoid displacement point for each frame.

Quantification of hyoid displacement, or the change from resting hyoid distance to maximal displacement distance, was calculated as a percentage of the distance travelled from rest

( $\text{maxdistance} - \text{restdistance} / \text{restdistance}$ ), and also as absolute value of distance travelled. Both were used for analysis to elucidate the more reliable method.

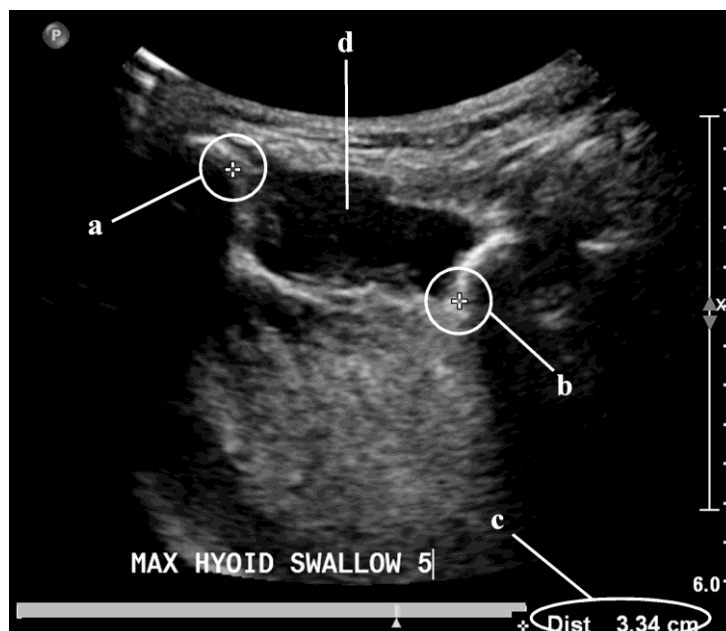


Figure 5.2. Sonogram of the hyoid/spine of mandible distance at the point of maximal displacement. Note the thickening of the geniohyoid muscle (**d**) during maximal displacement. While the caliper mark at the mental spine of the mandible (**a**) remains the same as the rest position, the caliper denoting the hyoid shadow (**b**) has shifted anteriorly towards the mental spine of the mandible.

#### 5.2.4 Statistical analysis

Statistical analysis was performed using Predictive Analytics SoftWare (PASW, SPSS Release 18.0). Inter- and intra-rater reliability were analysed using the intra-class correlation coefficient (ICC) using an absolute agreement definition. As the focus was on level of agreement between raters rather than between participants, measurements from each rater, of each of the five swallows from each of the five participants were included in the analysis. Therefore 25 ratings were compared for absolute agreement for each measure (rest, maximal displacement, percent change, and absolute change). Intra-rater reliability was calculated from measures made by the primary investigator only. For this, the primary investigator measured all 25 swallows from the 5 participants on two separate occasions. Inter-rater reliability was calculated from the measures obtained from the three raters. The following ICC analyses were completed for both inter-rater and intra-rater reliability assessment:

1. Distance between hyoid and mandible at rest
2. Distance between hyoid and mandible at maximal displacement
3. Percent change of hyoid position from rest to maximal displacement
4. Absolute change of hyoid position from rest to maximal displacement

### 5.3 Results

The range of the distance between the hyoid and mandible calipers was 4.6 – 5.9 cm at rest and 3.1 – 3.9 cm at maximum displacement. Single-measure intra-class correlation coefficients (ICCs) for inter-rater reliability are shown in Table 5.1. ICCs for intra-rater reliability are shown in Table 5.2. ICCs were high for inter-rater agreement at .86 for measures of resting distance of hyoid to mandible and .90 for measures of maximal displacement. Intra-rater reliability was even higher at .95 for measures of resting distance and .98 for maximal displacement measures.

The range for the percentage change from rest to maximal displacement was 17 – 44%. The range for the absolute change of hyoid position was 0.8 – 2.6 cm. Regarding the reliability of quantification of hyoid movement, the inter-rater ICC for percent change of hyoid position was greater than that for absolute change of hyoid position at .76 and .69, respectively. This was also the case for intra-rater ICCs at .93 and .90, respectively.

**Table 5.1. Single-measure intra-class correlation coefficients (ICCs) for inter-rater reliability**

		Inter-rater ICC	F	<i>p</i> -value
Distance between hyoid and mandible	At rest	.86	19.58	< 0.001
	Maximal displacement	.90	27.78	< 0.001
Change in hyoid displacement	% change	.76	10.41	< 0.001
	Absolute change	.69	7.82	< 0.001

**Table 5.2. Single-measure intra-class correlation coefficients (ICCs) for intra-rater reliability**

		<b>Intra-rater ICC</b>	<b>F</b>	<b><i>p</i>-value</b>
Distance between hyoid and mandible	At rest	.95	38.52	< 0.001
	Maximal displacement	.98	95.68	< 0.001
Change in hyoid displacement	% change	.93	27.41	< 0.001
	Absolute change	.90	19.12	< 0.001

## 5.4 Discussion

This preliminary study investigated the viability of a novel method of data analysis using ultrasound to quantify hyoid movement. This method utilized an anatomical reference point in order to eliminate the need for complex data transformation and calibration, and to provide a constant reference by which transducer movement can be monitored. These data suggest that raters can achieve high agreement regarding measures of maximal hyoid displacement during swallowing when reviewing the same ultrasound swallowing sweeps. Although the measurements at rest and maximal displacement taken by each rater were highly correlated, there was a small reduction in agreement of percent change and agreement of absolute change from rest to maximal displacement. This suggests that distances were measured by raters in a similar fashion; that is, larger distances were measured as such by each rater but that the actual values of the measures differed slightly from rater to rater. The fact that percent change was more highly correlated than absolute change suggests that by normalizing values to the reference point, some of the variance in measurement is reduced. As this preliminary study presents data using a small number of samples, further validation of this novel method is required.

While inter-rater reliability of measures of change was lower than the measurements at rest and maximal displacement, intra-rater measures of change remained high. This suggests that definition of caliper placement may vary slightly from rater to rater but, within a rater, definition of caliper placement remains more consistent.

Although the method of analysis evaluated in this study was measured with a high degree of reliability, further investigation is needed to assess the confounding intra-rater and intra-participant variability in data acquisition. Unlike some previous investigations of hyoid movement that have utilized ultrasound (Chi-Fishman & Sonies, 2002a, 2002b), this study did not stabilize participants' heads or the transducer during the acquisition of swallowing sweeps. Instead, the present study employed a reference point (mental spine of mandible), in an attempt to eliminate the effects of transducer movement on displacement values and therefore remove the need for cumbersome and expensive stabilization devices. However, because each rater analyzed the sonograms taken by a single rater and was not required to acquire the video sweep independently, it would be desirable for the reliability of the entire process to be determined for future applications in both research and clinical settings. It is possible that variation of participant positioning would reveal the need for head and transducer stabilization. This may be especially pertinent for data acquired over different sessions, when maintenance of positioning cannot be ensured.

The use of ultrasound to document hyoid displacement in the clinical setting warrants further discussion. Whether hyoid displacement is sufficient for effective swallowing is determined by observation of the ensuing effects, particularly epiglottic deflection and opening of the UES. However, as ultrasound does not allow visualization of these biomechanical events, it is necessary to establish whether this method is useful for evaluation of disordered swallowing function in the absence of normative data acquired during unimpaired swallowing. It may be that individual variation in hyoid displacement makes documenting norms an ineffectual undertaking, but further assessment of reliability of measures taken would assist in resolving this concern.

Alternatively, if ultrasound is shown to be sensitive to changes in hyoid displacement as a result of swallowing rehabilitation techniques, intra-participant comparisons may prove clinically useful. Ultrasound may also provide a useful adjunct to videofluoroscopy in allowing correlation of ultrasound measures with biomechanical observations on videofluoroscopy, and changes in swallowing function. More frequent assessment of hyoid displacement can be carried out in between videofluoroscopic evaluations of swallowing using ultrasound.



In summary, this novel method of analysis appears to provide a useful approach to the measurement of hyoid displacement during swallowing, eliminating the need for complex data calibration and transformation. Using percent change of hyoid displacement from resting position may offer a more reliable measure than absolute change. Further evaluation of the reliability of the entire process of data acquisition without stabilization devices should be completed before ultrasound can be incorporated into clinical assessment of swallowing disorders.



## **Chapter 6: Cross-sectional area of the submental muscle group: An ultrasound and MRI study**

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### **6.1 Introduction**

Muscle morphometry has been assessed using a variety of imaging techniques, including MRI (Aagaard, et al., 2001; Kubo, et al., 2006; Narici, et al., 1992; Robbins, et al., 2005; Robbins, et al., 2007; Stonecipher, et al., 1994), computed tomography (CT) (Engstrom, et al., 1991; Hudash, et al., 1985; Sipila & Suominen, 1993, 1995) and ultrasonography (Hodges & Gandevia, 2000; Maganaris, et al., 2002; Reimers, et al., 1998; Reimers, et al., 1996; Scholten, et al., 2003; Sipila & Suominen, 1991, 1996; Stonecipher, et al., 1994; Watkin, et al., 2001; Weiss, et al., 1988). The use of radiographic imaging when investigating muscle size in non-patient populations poses an ethical barrier to research, thus encouraging the use of techniques that rely on non-invasive methods. While MRI eliminates this exposure, it presents a costly method of investigation for researchers. Ultrasound provides another method of investigating muscle size, eliminating many issues that surround the use of CT and MRI.

While two-dimensional calculations made with ultrasound are reportedly reproducible for swallowing muscles (Emshoff, et al., 1999), and valid for limb muscles (Miyatani, et al., 2004), no studies have compared submental muscle CSA measures made from ultrasonographic and MRI images to determine if image quality is compromised when utilizing the former, as reported for other muscles (Juul-Kristensen, et al., 2000a; Schedel, et al., 1992). The aim of the current study was to compare the cross-sectional area of the submental muscles obtained using ultrasound to that acquired with MRI. By assessing the capability of ultrasound to demarcate these muscles, we wished to determine if it could provide a valid method of documenting CSA of the submental muscles. If ultrasound can provide this information, changes in oral musculature that result from factors such as exercise and atrophy secondary to disease or aging can be investigated with reduced cost and time compared with MRI.

## **6.2 Method**

### **6.2.1 Participants**

11 healthy volunteers (2 males and 9 females, aged between 20-42 years) were recruited for one session. Participants had no history of surgery or disease affecting the head and neck musculature. Ethical approval was obtained from the appropriate regional health research ethics committee, and informed consent was obtained prior to commencement of data collection.

### **6.2.2 Procedure**

MRI — 3D coronal oblique T2-weighted images (TE/TR = 87.8/3000 ms, TI = 0 ms, flip angle = 90 deg, acquisition matrix = 288 x 192 x 36, Reconstruction matrix = 512 x 512 x 36, FOV = 160 x 160 mm<sup>2</sup>, slice thickness = 3 mm, voxel size = 0.31 x 0.31 x 3.00 mm<sup>3</sup>) were acquired on a 3-T GE (GE Healthcare, Wisconsin, USA) HDx scanner with an 8-channel head coil. Participants were supine in the MRI scanner, with the head and neck placed within the head coil fixed to the scan table. Participants were asked to remain stationary and inhibit swallowing for the duration of the 3 min scan.

Ultrasound — A Philips (Philips Healthcare, Surrey, UK) IU22 ultrasonography instrument was used with a 12–5 MHz linear array transducer to acquire grey-scale images of the submental muscles in a coronal plane. Images of the submental muscles were acquired with the participant sitting upright. Participants were instructed to sit comfortably and relax their head in a neutral position. Once the participant achieved this posture, they were asked to maintain it while the transducer was placed under the chin, and not to accommodate the transducer with flexion of the neck. A generous amount of Aquasonic 100 ultrasound conductive gel was placed over the transducer, which was then placed perpendicular to the submental muscle group, with minimal pressure to ensure that transducer pressure did not distort muscle structure (Scholten, et al., 2003). The transducer was placed in a coronal plane, approximately midway between the mentalis of the mandible and the superior palpable edge of the thyroid cartilage. Depth settings were tailored to accommodate individual anatomy, and gain settings were adjusted to allow optimal visualization of muscle borders. Measures were derived for both techniques off-line.

### 6.2.3 Data analysis

All images were imported into the DICOM viewing software Osirix™. The zoom function was used to enlarge the muscles of interest to approximately the same size on both the MRI and ultrasound images. The geniohyoid and mylohyoid muscle boundaries could not be visualized sufficiently to allow measurement from MRI images, thus analysis was limited to anterior belly of digastric. For MRI, the midslice (in the case of an odd total of slices) or the two midslices (in the case of an even total number of slices) of the scan were used to calculate CSA. The midslice(s) was used in an attempt to measure the same muscle section imaged using ultrasound. Continuous trace calipers were used to make CSA measures of both the left and the right bellies of the anterior belly of the digastric muscle.

### 6.2.4 Statistical analysis

Means and standard deviations were calculated for each anterior belly of the digastric for both methods. A linear mixed-effects model (Gelman & Hill, 2007; Pinheiro & Bates, 2000) was used to compare values obtained by ultrasound and MRI for the left and right anterior belly of digastric muscle. Pearson correlations were used to determine the relationship between the measures obtained by the two methods.

## 6.3 Results

The mean ( $\pm$ SD) CSAs ( $\text{cm}^2$ ) derived from MRI were  $0.96 \pm 0.23$  (left) and  $0.97 \pm 0.27$  (right), and from ultrasound were  $0.87 \pm 0.19$  (left) and  $0.86 \pm 0.21$  (right). A scatterplot of the values for the left and right anterior bellies is shown in Figure 6.1. Ultrasound CSA measures were smaller than MRI measures ( $p = 0.01$ ) by 10% (95% CI: -18% – -2%). There was no evidence of a difference ( $p = 0.96$ ) between the left and right muscles (95% CI: -4% – 4%). Pearson correlations for both the left ( $r = .909$ ) and right ( $r = .776$ ) measures of CSA by MRI versus ultrasound were significant ( $p < 0.001$  and  $p = 0.005$ , respectively).

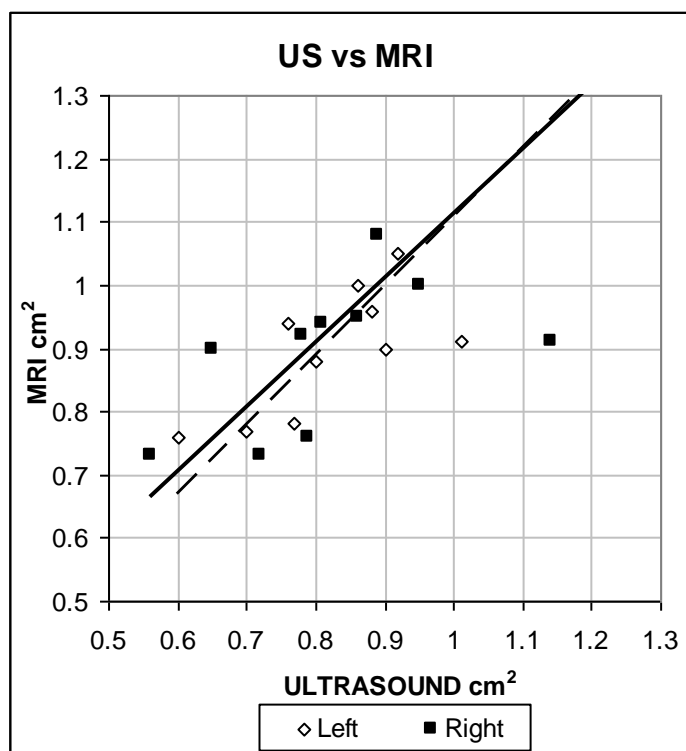


Figure 6.1. Scatterplot comparing values for ultrasound with MRI for both the left and right anterior belly cross sectional area (CSA). Dashed line represents the line of best fit for CSA measures of the left belly, and the solid line represents the right. MRI values are on the Y axis, ultrasound values on the X axis.

## 6.4 Discussion

This is the first study to correlate CSA measurement of the submental muscles acquired using ultrasound with MRI acquired measures. The results suggest that CSA measures of the anterior digastric muscles acquired from ultrasound images are highly correlated with those obtained from ‘gold standard’ images from MRI. Furthermore, ultrasound was found to be superior in some aspects of measurement, thus calling into question the application of MRI for quantification of CSA of these specific muscles. Overall, results from this study provide confidence in the use of ultrasound for measurement of the submental muscle group.

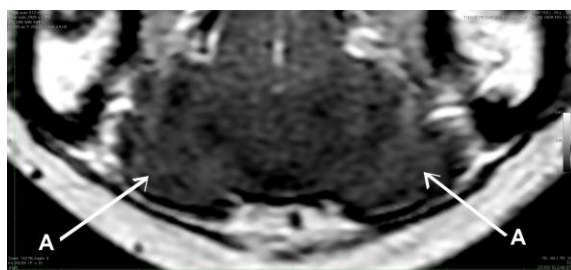
Warranting consideration is the fact that mean CSA values from MRI images exceeded those from ultrasound images by approximately 10%. The possible contributing factors include differences in the technical set up of the two techniques, positioning during image acquisition, and image clarity. Technical considerations may involve calibration error in either the MRI or ultrasound instrumentation, resulting in inaccurate absolute image dimensions. While this is a

possibility, differences in image clarity and/or participant positioning most likely explain the discrepancy. Inspection of Figure 6.1 shows that the increase in CSA measured from MRI images is not systematic, with three instances having larger ultrasound values than MRI. One of these has a minimal difference of  $0.03 \text{ cm}^2$ , suggesting the CSA obtained from both measures is almost identical. Interestingly, the two remaining data points with values larger from ultrasound than MRI are taken from the same participant. This suggests that something specific to this participant resulted in increased CSA measures from ultrasound images. This could be related to the composition of fatty tissue and muscle, and/or an interaction with either the transducer placement in the ultrasound image acquisition or positioning in the MRI scanner. As all other measures made from MRI images were identical (1 data point) or larger (18 data points), exploration of factors possibly contributing to systematic increases in CSA for MRI measures is worthy of consideration.

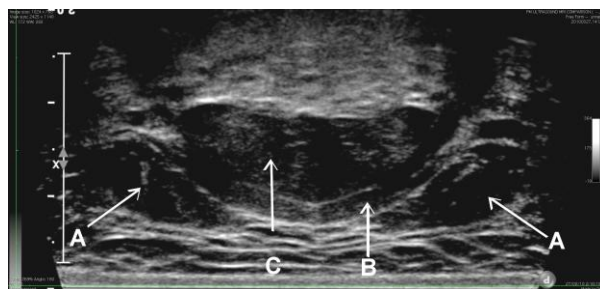
The positioning of participants varied across methods in the present study. Participants were seated upright with their head in a neutral position for ultrasound, while supine for MRI. The head coil used for MRI imaging dictates head position to some extent, possibly decreasing the length of the submental muscle group. Post-hoc analysis of MRI images showed CSA of the anterior belly to increase posteriorly and decrease anteriorly from the midslice. This tendency for an increase in CSA towards the superior palpable edge of the thyroid cartilage, rather than a maximal CSA at the muscle belly, may suggest positioning of participants substantially deformed the muscle during MRI scans. As ultrasound images were only taken at the midway point between the mentalis of the mandible and the superior palpable edge of the thyroid cartilage, this assumption cannot be confirmed, but should be considered when contemplating sources of variance seen in MRI data of the neck muscles.

CSA measures of the geniohyoid muscle and thickness measures of the mylohyoid muscle were not possible on MRI images due to poor border delineation (Figure 6.2 and 6.3). These muscles could be differentiated and measured from ultrasonographic images, suggesting a difference in the sensitivity of the two methods for demarcating these muscles. As discussed in Section 3.3.2, the acquisition of MRI images requires a longer duration of movement inhibition than ultrasound image acquisition. As the submental muscles are activated during swallowing at least once every minute (Rudney, et al., 1995), it is likely image clarity was compromised to a greater degree for MRI than ultrasound. CSA measures were taken from the

muscle belly in both ultrasound and MRI images. As most movement occurs at the muscle belly, controlling movement is essential for CSA measures from this location, suggesting the advantage of rapid acquisition time of ultrasound is especially applicable in this case. Difference in signal generation between the two methods may also contribute to the superior image quality documented for ultrasound in this study. As discussed in Section 3.3.2, because ultrasound uses the change in reflective properties of adjacent tissues, it may be more sensitive to the muscle borders in this confined space compared with MRI which generates a signal based on proton density. Additionally, because of scanning schedules and limited funding associated with the MRI image acquisition; it was only possible to scrutinize and repeat image acquisition if movement artifact was detected during the ultrasound procedure.



*Figure 6.2. Coronal image of the submental muscle group obtained using MRI. Anterior bellies of digastric are labelled A.*



*Figure 6.3. Coronal image of the submental muscle group obtained using ultrasound: Anterior bellies of digastric are labelled A, mylohyoid labelled B, and geniohyoid muscles labelled C.*

As these results suggest valid measures of anterior digastric CSA can be obtained using ultrasound, the repeatability of measures needs further attention if ultrasound is to be used to document changes in muscle morphometry across sessions. Emshoff and colleagues' (1999) investigation into the reliability of ultrasound measures of the anterior belly of the digastric muscle included a time lapse of more than 5 min between image acquisitions. Further research is required to look at the reliability and also the precision of ultrasound measures in this muscle group obtained with a longer period of time between sessions. Documenting the



variance associated with a longer time lapse between sessions will assist with determining the magnitude of effects required to override such variance. To validate the sensitivity of ultrasound in detecting such changes, longitudinal research with an expected outcome of modified muscle morphometry is also required. Comparison of results obtained over repeated measures from both ultrasound and MRI is necessary to further clarify sources of variation specific to each method.

MRI and ultrasound measures of CSA of the digastric muscle are highly correlated, although MRI images have a larger group mean. Ultrasound has the advantages of natural participant positioning, superior clarity of muscle borders of all of the submental muscles, requires less acquisition time, and is a much less expensive method of examination to that of MRI. In summary, this study has shown that ultrasound is a viable imaging modality for quantitative measures of the submental muscle group and provides advantages over MRI beyond cost and accessibility.



## **Chapter 7: Reliability of motor evoked potentials: Comparison of methods**

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### **7.1 Introduction**

Motor evoked potentials (MEPs) induced with transcranial magnetic stimulation (TMS) have been used to assess corticomotor projections to most accessible muscles in the human body. MEPs are used to investigate a variety of components of corticomotor function including size of cortical representation of the target muscle, motor threshold, cortical ‘hotspot’ for optimal stimulation, excitability of the corticomotor pathway, conduction time from the cortex to the muscle, intracortical facilitation, and intracortical inhibition. While many studies have investigated these measures using MEPs, there is no clear consensus regarding the optimal method of quantifying MEP responses for such assessments (Awiszus, 2005).

Various methods have been reported for quantification of MEP amplitudes, including the mean peak-to-peak value of multiple MEPs (Dishman, Greco, & Burke, 2008; Doeltgen, et al., 2010a; Gow, et al., 2004b; Jefferson, et al., 2009a; Mistry, et al., 2007), median peak-to-peak value of multiple MEPs (Awiszus, 2005; Wolf, et al., 2004), peak-to-peak value of ensemble-average MEP waveform (Awiszus, 2005; Bastings, et al., 2002; McDonnell, et al., 2004; Pitcher & Miles, 2002; Pitcher, et al., 2003), peak-to-peak value of an ensemble-median MEP waveform (Awiszus, 2005), maximal peak-to-peak value of multiple MEPs (McDonnell, et al., 2004), and area of multiple rectified and averaged MEPs (Doeltgen, et al., 2011; McDonnell, et al., 2004; Ziemann, et al., 1999). Despite the number of different approaches, very few studies compare results from the different methods (Awiszus, 2005; McDonnell, et al., 2004).

A study by McDonnell et al. (2004) looked at MEP amplitude values from the first dorsal interosseous (FDI) muscle of the hand and the flexor carpi ulnaris (FCU) muscle of the forearm across two sessions. The study assessed both peak-to-peak amplitude and area of MEPs using three different extraction methods: mean values of multiple MEPs, values from the ensemble-average waveform, and values from the maximal MEP response. When making comparisons between the ensemble-average values and the mean values, they showed that while ensemble-average values were significantly smaller than the mean values, the peak-to-

peak amplitudes and areas from these two methods were highly correlated. Furthermore, the ICCs across the two sessions for mean and ensemble-average methods were almost identical, both achieving ‘poor’ to ‘moderate’ reliability (Portney & Watkins, 2009). While McDonnell and colleagues acknowledge that, unlike the mean values, the unrectified ensemble-average waveform can result in phase cancellation and, therefore, smaller amplitudes and area, this does not appear to adversely influence the reliability of the ensemble-average method or the correlation between the ensemble-average and mean values. The authors suggested similar investigations of MEPs from other muscles are warranted to see if these findings translate to MEPs recorded from other muscles.

A problem with deciphering which of the analysis methods from the McDonnell et al. study is optimal is that the ‘gold standard’ result is uncertain. Increased reliability could be derived from MEP values that are more similar due to being either more accurate or less accurate. Only a study by Awiszus (2005) has completed a similar exploration of MEP extraction methods to that of McDonnell et al. (2004). It deviates from McDonnell et al.’s approach by using an objective measure by which the extraction methods can be compared. Additionally, Awiszus incorporates two additional methods: median peak-to-peak values from multiple MEPs and peak-to-peak value of the ensemble-median MEP waveform. He credits the basis for these additions to Wolf et al. (2004), who used a median value to minimize the influence that outliers have on the averaged MEP amplitudes. The methods of analysis were assessed against an input-output curve developed by Awiszus according to the IFCN guidelines using a “threshold success definition” (for review see Awiszus, 2005, p. 5). MEP amplitudes obtained from each extraction method were plotted against this “threshold success definition input-output curve” (Awiszus, 2005, p. 5) to assess which method provided values most consistent with the threshold concept of the IFCN guidelines. Interestingly, this study concluded that reporting the median values of multiple MEPs, but not the other methods, replicates the same underlying concept as the threshold concept described by the guidelines, suggesting an advantage of this technique over averaging techniques or the use of an ensemble-median waveform.

The aim of the current study was to assess the reliability of various methods of submental MEP analysis across five recording blocks and to determine the relationship between the various methods. Additionally, variance at both the group and within-participant levels is

reported to provide precision estimates of each method (see Section 3.6, pages 79-83 for definitions of reliability and precision).

## **7.2 Method**

### **7.2.1 Data**

A pre-existing data set was used for this study. The data included five MEP recording blocks obtained over a two-hour period from each of six different healthy participants. 15 MEPs were included in each recording block. The data used in this study were collected as a ‘control’ condition in a study designed to assess whether MEPs from the submental muscles are subject to order effects unrelated to treatment. The data for the original study were extracted as the average peak-to-peak values of 15 MEPs. These results are presented elsewhere (Al-Toubi, et al., 2010), showing no significant differences across the five recording blocks when analysed with GLM-RM ANOVA.

The instrumentation used for obtaining MEPs in this study was the same as reported in Section 12.2.1 of this thesis. Procedures are described in Section 12.3.2. Following the collection of 15 baseline MEPs obtained during volitional contraction of the submental muscles, participants were asked to remain relaxed for 25 min. Immediately following the 25 min of relaxation, another set of 15 MEPs were collected, with further sets recorded at time points 30, 60 and 90 min, as described in Section 12.3.7. Therefore, five blocks of 15 MEPs were obtained from each participant: baseline, <5 min, 30 min, 60 min, and 90 min following relaxation. This analysis utilized only the MEPs obtained during volitional contraction of these muscles, as described in Section 12.3.2.

### **7.2.2 Analysis software**

Data were analysed using the University of Canterbury Evoked Potential Analysis software version 3.15<sup>18</sup>, a custom-designed software package which allows quantification of onset latency (magnetic stimulus – onset of MEP), peak-to-peak amplitude, and area of the MEP. The software displays each MEP as an individual waveform, with options for displaying an ensemble-average or ensemble-median waveform (Figure 7.1) of multiple MEPs, or rectified

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<sup>18</sup> University of Canterbury Evoked-Potentials Analysis Software, G. A. O’Beirne, University of Canterbury, Christchurch, New Zealand, 2010

average of multiple waveforms. Onset and offset latency markers can be subjectively placed (Figure 7.1), or objectively placed according to specified criteria (Figure 7.2). The criteria for objective onset threshold breach can include a specified standard deviation above the pre-stimulus baseline EMG signal. Within the onset and offset markers, the software calculates the amplitude between the highest positive peak and the lowest negative peak for peak-to-peak amplitude, or area in the case of rectified MEPs. The software allows high- and low-pass filtering using a variety of filters and orders. The peak-to-peak amplitude or area and onset latency values are saved as a Microsoft Excel data sheet by the researcher for analysis.

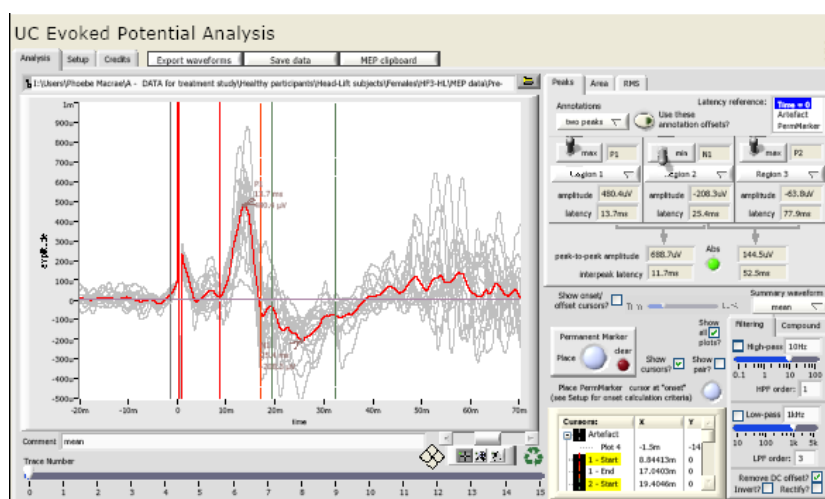


Figure 7.1. MEP waveforms displayed in the UC Evoked Potential Analysis software. The first thick vertical red line represents the discharge of the magnetic stimulus. The ensemble-average waveform is trace 0 and is represented by the red waveform. The remaining 15 traces are the 15 MEPs. The remaining two red vertical cursors represent the region in which positive peak amplitude will be calculated, and the green cursors represent the region for negative peak amplitude. Peak-to-peak amplitude is displayed at the top right of the screen. By setting the first cursor that defines the region for the positive peak at the onset of the MEP, the onset latency is displayed in the cursor description column on the right lower section of the screen.

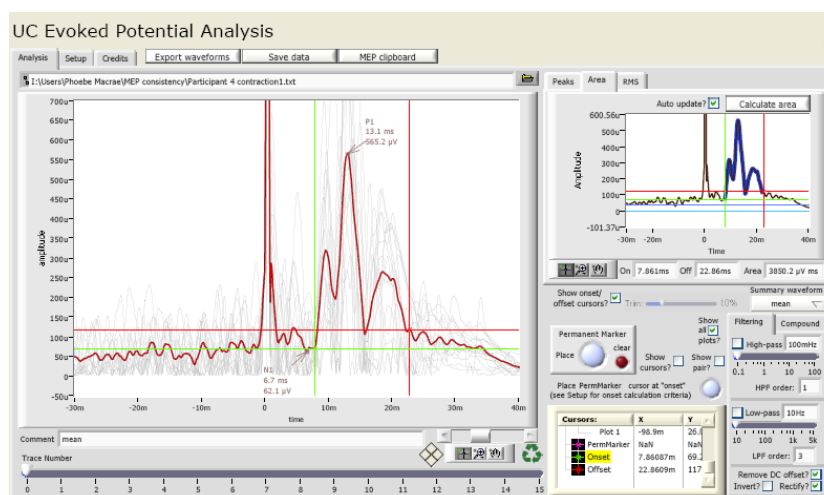


Figure 7.2. Objective cursor placement can be achieved through specifying onset threshold criteria. This can be completed on rectified (as seen in the figure above) or unrectified waveforms. The window in the upper right corner of the screen displays the section of waveform used to calculate the area in blue. A 15 ms duration encompasses the MEP response (see method K below).

### 7.2.3 Data analysis

Six methods were used to quantify onset latency in this investigation:

- A. Mean latency - The researcher set the onset latency marker for each individual waveform at the beginning of the peak subjectively deemed to be MEP onset. The 15 onset latency values were then averaged such that mean onset latency was derived for all five time points for each of the six participants.
- B. Median latency - To assess the effects of outliers in the set of 15 individual MEPs, the median value of the 15 trials was evaluated (Awiszus, 2005; Wolf, et al., 2004). For this method, the median value of the 15 onset latencies was derived for all five time points for each of the six participants.
- C. Ensemble-average latency - To assess the variance introduced by assessing each MEP waveform individually, the ensemble-average waveform generated by the software for each of the five recording blocks was evaluated (Bastings, et al., 2002; McDonnell, et al., 2004; Pitcher & Miles, 2002; Pitcher, et al., 2003). For this method, the researcher set the onset latency marker at the beginning of the peak subjectively deemed to be the onset of the ensemble-average waveform at each time point.

- D. Ensemble-median latency - To assess the effects of outliers on the ensemble-average waveform, the ensemble-median waveform generated by the software was evaluated (Awiszus, 2005). For this method, the researcher set the onset latency marker at the beginning of the peak subjectively deemed to be the onset of the ensemble-median waveform at each time point.
- E. Rectified and objective latency - To assess whether subjectively determining onset latency introduced bias in the reproducibility of onset latency values, single-trial rectification and averaging of the 15 individual waveforms was performed. The level of pre-stimulus sEMG was integrated over a period of 50 ms up to 5 ms prior to the magnetic stimulus (Doeltgen, et al., 2011; Ziemann, et al., 1999). The presence of an MEP was accepted if the post-stimulus sEMG exceeded the pre-stimulus sEMG by two standard deviations for at least 5 ms (Doeltgen, et al., 2011). Definition of onset latency was made automatically at the point at which the two standard deviation threshold was breached.

It should be noted that this analysis method could not be completed on all MEP blocks due to stimulus artefact following the magnetic stimulus (Figure 7.3). Numerous manipulations were required using high and low pass filtering of different levels so that each MEP onset would breach the 2 standard deviation threshold. Therefore, in practice, this method was not objective in nature due to the bias introduced by filtering MEPs that did not adhere to strictly objective criteria. This method was therefore disregarded.

- F. Rectified and subjective latency - As objective quantification of onset latency was not possible on the rectified waveforms, subjective measures were assessed. Single-trial rectification and averaging of the 15 MEPs was performed. The researcher then subjectively set the onset latency marker at the beginning of MEP. To control for the inclusion of non-MEP EMG, a criterion was set that post-stimulus EMG had to be greater than 2 standard deviations above the background EMG level (Doeltgen, et al., 2011). Note that this did not require the onset to breach this threshold but required the minimum value of the onset to be at least 2 standard deviations above the background EMG. The level of pre-stimulus sEMG was integrated over a period of 50 ms up to 5



ms prior to the magnetic stimulus to determine the 2 standard deviation level (Doeltgen, et al., 2011; Ziemann, et al., 1999).

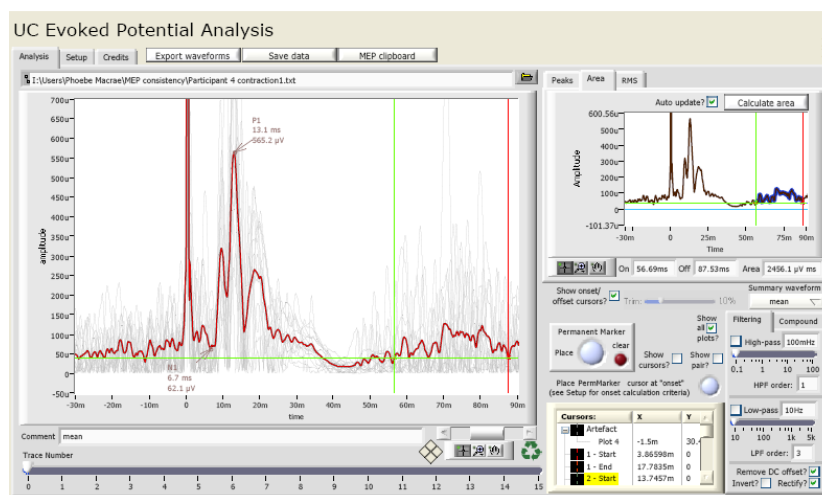


Figure 7.3. Example of failure of the objective onset latency detection on the rectified and averaged waveform due to stimulus artefact. The horizontal green line (in both windows) represents the 2 standard deviation threshold. As the post-stimulus baseline doesn't breach the threshold, the onset is not detected until after the MEP response.

Five methods were used to quantify MEP amplitude or area in this investigation:

- G. Mean amplitude - The researcher defined the regions containing the greatest positive and consecutive negative peaks for each of the 15 individual waveforms, within which the software calculated the amplitude. The 15 values were then averaged to obtain a mean amplitude value for each of the five time points.
- H. Median amplitude - To minimize the effects of outliers, the median value of the 15 individual trials was used as the amplitude value for each of the five time points (Awiszus, 2005; Wolf, et al., 2004).
- I. Ensemble-average amplitude - To assess the variance introduced by assessing each MEP waveform individually, the ensemble-average waveform generated by the software was evaluated for peak-to-peak amplitude (Bastings, et al., 2002; McDonnell, et al., 2004; Pitcher & Miles, 2002; Pitcher, et al., 2003). Regions containing the positive and negative peaks were subjectively defined by the researcher.

- J. Ensemble-median amplitude - To assess the effects of outliers on the ensemble-average waveform, the ensemble-median waveform generated by the software was evaluated for peak-to-peak amplitude (Awiszus, 2005); again, regions containing positive and negative peaks were subjectively defined by the researcher.
- K. Rectified area - To eliminate the effect of phase cancellation that occurs when utilizing the ensemble-average and ensemble-median waveforms (McDonnell, et al., 2004), the area of the averaged waveform of the rectified single trials was obtained. The researcher subjectively set the onset latency marker at the beginning of MEP (see method F). The offset cursor was then placed exactly 15 ms following the onset cursor (Sowman et al., 2009). This criterion has been used previously for MEPs from the submental muscle group (Sowman, et al., 2009). The 15 ms duration was an arbitrary choice made by the researchers based on visual inspection of their data (Nordstrom, M, A., personal communication, June 1, 2011). Visual inspection showed that this duration also corresponded to the typical EMG response in the current data set (Figure 7.2). Additionally, as contraction of the submental muscles is a volitional task, controlling the duration of EMG response included in the MEP may be necessary to ensure larger area is not achieved merely through longer contractions (see Section 3.1.1.3). The pre-stimulus EMG area was calculated over a 15 ms period prior to the magnetic stimulus (-22 – -7 ms, Figure 7.4), and subtracted from the post-stimulus MEP area (Doeltgen, et al., 2011; Pearce, Miles, Thompson, & Nordstrom, 2003; van Hedel, Murer, Dietz, & Curt, 2007), leaving the estimated area of the MEP.

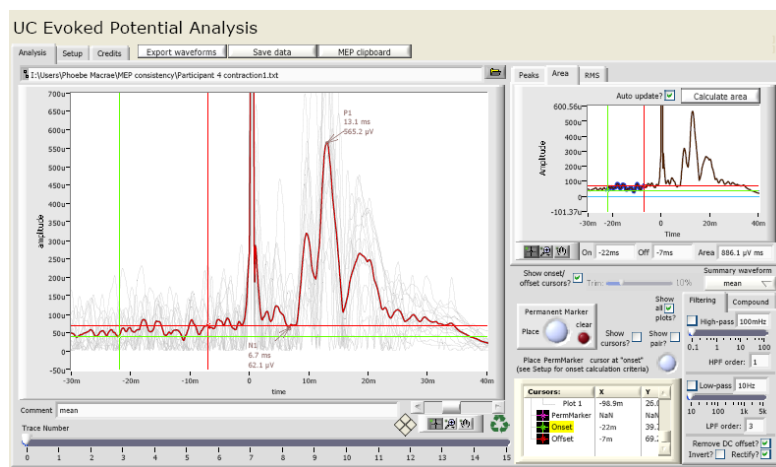


Figure 7.4. Calculation of the pre-stimulus area over a 15 ms period prior to the magnetic stimulus (-22 ms - -7 ms). This area was subtracted off the post-stimulus MEP response (calculated as described in Figure 7.2)

## 7.2.4 Statistical analysis

A repeated-measures analysis of variance (RM-ANOVA) was completed on latency and amplitude values using the SPSS statistics package (IBM, SPSS Release 19.0) to determine the effect of extraction method. Intra-class correlation coefficients (ICCs) using an absolute agreement definition were calculated to provide a reliability coefficient of each onset latency and amplitude extraction method. Means and standard deviations at the group and within-participant level were calculated to provide estimates of the precision of each method. Linear regression analysis was performed to investigate the relationship between all methods. Mauchly's test indicated that the assumption of sphericity had been violated for the main effect of method,  $\chi^2(9) = 28.50$ ,  $p < .01$ , and session,  $\chi^2(9) = 28.02$ ,  $p < .01$ , for the ANOVA completed for onset latency values. Therefore degrees of freedom were corrected using the Greenhouse-Geisser estimates of sphericity ( $\epsilon = .37$  for the main effect of method and .43 for the main effect of session).

## 7.3 Results

### 7.3.1 The effect of extraction method

#### 7.3.1.1 Onset latency methods

There was no effect of session ( $F(1.73, 8.62) = .28$ ,  $p = 0.74$ ,  $\eta_p^2 = .05$ ), or method\*session ( $F(16, 80) = 1.29$ ,  $p = 0.22$ ,  $\eta_p^2 = .21$ ), implying that there were no order effects for onset latency values for any of the five latency estimation approaches. There was a main effect of extraction method for onset latency ( $F(1.49, 7.46) = 7.11$ ,  $p = 0.02$ ,  $\eta_p^2 = .59$ ). Means and standard deviations are shown in Table 7.1. Results of post-hoc t-tests are shown in Table 7.4.

**Table 7.1. Mean values of the methods for quantifying MEP onset latency, group standard deviations, and within-participant standard deviations. Standard deviations are also reported as a percentage of the mean (in parentheses).**

Method	Mean	Group SD	Within-participant SD
A – Mean of 15 individual MEPs	9.98 ms	2.12 ms (21%)	0.86 ms (9%)
B – Median of 15 individual MEPs	9.97 ms	2.27 ms (23%)	1.06 ms (11%)
C – Ensemble-average waveform	8.41 ms	1.99 ms (24%)	0.68 ms (8%)
D – Ensemble-median waveform	8.66 ms	2.17 ms (25%)	0.72 ms (8%)
F – Rectified waveform	8.45 ms	1.56 ms (18%)	0.78 ms (9%)

### 7.3.1.2 *Amplitude/area methods*

Means and standard deviations are shown in Table 7.2. As the rectified area method (K) quantified MEP size in a unit different to all other methods ( $\mu\text{V}\cdot\text{ms}$ ), RM-ANOVA could not compare the measures made with this method to the others. The four other methods were analysed with the same RM-ANOVA. A separate RM-ANOVA was completed on the rectified waveform to assess the effect of session. There was no effect of session ( $F(4, 20) = .76, p = 0.57, \eta_p^2 = .13$ ) or method\*session ( $F(12, 60) = 1.68, p = 0.10, \eta_p^2 = .25$ ) for the four amplitude estimation approaches analysed with the same ANOVA, and no effect of session for the ANOVA completed on the rectified waveform data ( $F(4, 20) = .46, p = 0.77, \eta_p^2 = .08$ ), implying no order effect for amplitude values for any of the five amplitude estimation approaches. There was a main effect of extraction method on amplitude results from the ANOVA done on the four estimation approaches together ( $F(3, 15) = 31.05, p < 0.001, \eta_p^2 = .86$ ). Results of post-hoc t-tests are shown in Table 7.5.

**Table 7.2. Mean values of the methods for quantifying MEP amplitude and area, group standard deviations, and within-participant standard deviations. Standard deviations are also reported as a percentage of the mean (in parentheses).**

Method	Mean	Group SD	Within-participant SD
G – Mean of 15 individuals	789 $\mu\text{V}$	375 $\mu\text{V}$ (48%)	90 $\mu\text{V}$ (11%)
H – Median of 15 individuals	762 $\mu\text{V}$	361 $\mu\text{V}$ (47%)	106 $\mu\text{V}$ (14%)
I – Ensemble-average waveform	636 $\mu\text{V}$	333 $\mu\text{V}$ (52%)	83 $\mu\text{V}$ (13%)
J – Ensemble-median waveform	647 $\mu\text{V}$	345 $\mu\text{V}$ (53%)	91 $\mu\text{V}$ (14%)
K – Rectified waveform	2685 $\mu\text{V}/\text{ms}$	1678 $\mu\text{V}\cdot\text{ms}$ (62%)	365 $\mu\text{V}\cdot\text{ms}$ (14%)

## 7.3.2 Reliability

### 7.3.2.1 *Onset latency methods*

Single-measure absolute agreement ICCs are presented in Table 7.3. The highest reliability coefficient was obtained using the ensemble-median latency method (D). The lowest reliability coefficient was obtained for the rectified and subjective latency method (F).

Precision estimates shown in Table 7.2 show the rectified and subjective method (F) is most sensitive to group treatment effects, and the ensemble-median onset latency method (D) is the

least sensitive. The mean onset latency method (A) is most sensitive to treatment effects revealed using a within-participant design, and the median onset latency method (B) is the least sensitive.

### 7.3.2.2 *Amplitude/area methods*

Single-measure absolute agreement ICCs are presented in Table 7.3. All amplitude estimation methods obtained reliability coefficients that were near identical. The highest reliability was for the rectified area method (K) and the mean amplitude method (G). The lowest reliability coefficient was for the median amplitude method (H).

Precision estimates presented in Table 7.2 show the median amplitude method (H) is most sensitive to treatment effects at a group level, and the rectified area method (K) is the least sensitive. The mean amplitude method (G) is the most sensitive to treatment effects using a within-participant design, with all other methods almost identical in their sensitivity, with precision estimates ranging from 13% - 14%.

**Table 7.3. Reliability coefficients (ICCs) for each extraction method.**

<b>Onset latency extraction method</b>		<b>Amplitude/area extraction method</b>	
A - mean onset latency	.78	G - mean amplitude	.95
B - median onset latency	.73	H - median amplitude	.92
C - ensemble-average onset latency	.84	I - ensemble-average amplitude	.94
D - ensemble-median onset latency	.86	J - ensemble median amplitude	.93
F - rectified subjective onset latency	.56	K - rectified area	.95

### 7.3.3 **Relationships between the various methods**

#### 7.3.3.1 *Onset latency methods*

Post-hoc t-tests between all methods of onset latency estimation are presented in Table 7.4. A Bonferroni corrected significance value of 0.005 is required to suggest significance at the 0.05 alpha level given the 10 comparisons made from the onset latency data (Bland & Altman, 1995). These analyses indicate that there is a difference in latency values between method A (mean latency) and all other methods except for method B (median latency), with method A having a longer onset latency than method C, D, and F (see Table 7.1). There was also a

difference between method B and the other methods, again with method B having a longer onset latency than methods C, D, and F. Methods C, D, and F (ensemble-average, ensemble-median, and rectified waveform) produced values that did not differ significantly from each other.

Linear regression analyses between all methods of onset latency estimation are also presented in Table 7.4. This shows high correlations between all measures, with the relationship between the ensemble-median latency (D) and the mean latency (A), and between the ensemble-median latency and the median latency (B) being the lowest, at  $r = .68$ .

**Table 7.4. Post-hoc t-test and correlation results comparing methods of quantifying onset latency**

Comparison	Post-hoc t-tests			Regression		
	Mean difference	t	p	r	F	p
<b>A vs. B</b>	0.01 ms	.13	0.90	.98	610.1	<.001
<b>A vs. C</b>	1.57 ms	5.88	<.001	.75	35.9	<.001
<b>A vs. D</b>	1.32 ms	4.17	<.001	.68	23.5	<.001
<b>A vs. F</b>	1.53 ms	6.23	<.001	.77	41.8	<.001
<b>B vs. C</b>	1.56 ms	5.81	<.001	.77	40.9	<.001
<b>B vs. D</b>	1.31 ms	4.04	<.001	.68	24.6	<.001
<b>B vs. F</b>	1.52 ms	5.63	<.001	.76	38.7	<.001
<b>C vs. D</b>	-.25 ms	-1.94	0.06	.95	240.7	<.001
<b>C vs. F</b>	-.04 ms	-.16	0.87	.79	45.2	<.001
<b>D vs. F</b>	.21 ms	.90	0.38	.80	50.8	<.001

### 7.3.3.2 *Amplitude methods*

Post-hoc t-tests between methods of amplitude estimation are presented in Table 7.5. A Bonferroni corrected significance value of 0.006 is required to suggest significance at the 0.05 alpha level given the 8 comparisons made from the amplitude data (Bland & Altman, 1995). Note that t-tests were not used to compare the rectified area method (K) with any other methods due to the different units expressed by this method. These analyses indicate that there was a difference in amplitude values between all methods except between method I (ensemble-average waveform) and method J (ensemble-median waveform). The means (Table

7.2) indicate that the ensemble-average and ensemble-median waveforms have smaller amplitude than the mean or median values calculated from 15 MEPs.

Linear regression analyses between all methods of amplitude/area estimation are also presented in Table 7.5. This shows high correlations between all the measures of amplitude estimation, including between the rectified area and all methods of peak-to-peak quantification.

**Table 7.5. Post-hoc t-tests and correlation results comparing methods of quantifying amplitude/area**

<b>Comparison</b>	<b>Post-hoc t-tests</b>			<b>Regression</b>		
	<b>Mean difference</b>	<b>t</b>	<b>p</b>	<b>r</b>	<b>F</b>	<b>p</b>
<b>G vs. H</b>	28 $\mu$ V	2.97	0.006	.99	1568.1	<.001
<b>G vs. I</b>	153 $\mu$ V	9.63	<.001	.98	582.2	<.001
<b>G vs. J</b>	143 $\mu$ V	8.29	<.001	.97	433.0	<.001
<b>G vs. K</b>	NA	NA	NA	.93	170.9	<.001
<b>H vs. I</b>	126 $\mu$ V	7.64	<.001	.97	440.6	<.001
<b>H vs. J</b>	115 $\mu$ V	7.20	<.001	.97	451.1	<.001
<b>H vs. K</b>	NA	NA	NA	.92	150.0	<.001
<b>I vs. J</b>	-11 $\mu$ V	-1.52	0.139	.99	2438.7	<.001
<b>I vs. K</b>	NA	NA	NA	.95	248.2	<.001
<b>J vs. K</b>	NA	NA	NA	.94	224.9	<.001

## 7.4 Discussion

The aim of this study was to determine the relative reliability of various MEP data extraction methods for MEPs recorded from the submental muscles following TMS. The relationship between the values obtained from each of the methods was also explored, as well as variance estimates to provide insight into the precision of each method. The extraction method affected the values obtained for both latency and amplitude/area quantification. Despite the different values, all measures were highly correlated, with most achieving similar estimates of reliability and precision.

Reliability across the five sessions ranged from “moderate” (.50 - .75) to “good” (>.75) (Portney & Watkins, 2009) for latency measures, and good for all amplitude/area methods (Portney & Watkins, 2009). Amplitude/area ICCs reported in the present study are higher than those reported for reliability of the mean of 15 submental MEPs across different sessions (.69) but similar to ICCs across trials from the same session (.92) reported by Doeltgen et al (2009a). This most likely reflects the fact that all five recording blocks in the present study were obtained on the same day, eliminating the need to replace recording electrodes. Reliability coefficients are higher than those reported for more distal muscles such as the FDI and FCU muscles (McDonnell, et al., 2004), an interesting finding based on the proposition that proximal muscles show more variability across trials compared to distal muscles (Brasil-Neto, McShane, Fuhr, Hallett, & Cohen, 1992).

The ensemble-median and ensemble-mean waveform methods produced the highest reliability coefficients for onset latency estimation, while all five methods for estimation of amplitude/area had very similar and high reliabilities. The least reliable measures were obtained from the rectified and subjective latency method and from the median amplitude method. Interestingly, the median amplitude is the method proposed to be the most consistent with the IFCN guidelines for quantifying MEP amplitude (Awiszus, 2005). This suggests that differences between the present study and the study by Awiszus, such as recording from different muscles or during rest rather than contraction, may contribute to this difference. Alternatively, it may suggest that the most accurate MEP values are in fact the most variable.

The lowest reliability coefficient for latency detection was obtained from the rectified waveform. The benefit of a rectified waveform or calculating latency from individual MEPs is that these methods eliminate biasing toward the latency values of the MEP with the shortest latency, which is inherent with unrectified ensemble-average or median waveforms. However, the present study found that the onset latency values obtained from the rectified waveforms did not differ significantly from the ensemble-average or ensemble-median waveform, with all three methods producing values smaller than those obtained from analysing each MEP individually. Therefore, the rectified waveform method appears to bias the onset latency as much as the ensemble-waveform method. Additionally, many studies subjectively select MEPs with the shortest onset latency from a set for analysis (Chang & Lin, 1999; Chen, Chen, Wu, Kao, & Liao, 1998; Chroni et al., 2011; Muellbacher, Artner, & Mamoli, 1998;



Tataroglu, Sair, Parlaz, & Deneri, 2011), suggesting the smaller values obtained by these three methods in the present study reflect values similar to those reported by other investigation of MEP onset latency.

The precision estimates show all methods have similar precision for both amplitude/area and onset latency estimates, for both group and within-participant values. These values give insight into the amount of change expected from simply repeating the measure. These estimates provide some guidance for interpreting effects that are either substantially smaller or larger than this variance when utilizing the same conditions as the current investigation. However, the small number of participants investigated, and the fact that all recording blocks were obtained on the same day must be considered when applying these precision estimates to further studies. The variance reported in the current study most likely overestimates the precision of studies that assess changes in MEP parameters over different days.

Despite significant differences across some methods of onset latency and amplitude/area detection, most methods were highly correlated with each other. The lowest correlations occurred for onset latency quantification, between the ensemble-median waveform and the mean value of 15 MEPs ( $r = .68$ ), and the ensemble-median waveform and the median value of 15 MEPs ( $r = .68$ ). Correlations between all amplitude/area quantification methods were high (no method being lower than  $r = .90$ ). This suggests that, regardless of which method is used, if within-subject changes in MEPs are of interest over repeated-measures, consistent use of any of the methods will provide similar results. This is further supported by the similar within-participant standard deviations obtained for all amplitude/area estimation measures. Despite phase cancellation possibly resulting in less ‘accurate’ values for the ensemble-average and ensemble-median methods, the similar reliability and precision estimates across these methods suggest this may not affect results. As ensemble waveforms are sensitive to phase cancellation, it was expected that their amplitudes would be smaller than values obtained from individual unrectified MEPs or rectified waveforms (McDonnell, et al., 2004). However, all methods of amplitude/area quantification differed significantly from each other, with the exception of the two ensemble waveforms, suggesting that researchers need to be aware of these influences when comparing results across studies utilizing different extraction methods.

No significant difference was noted for any onset latency or amplitude/area method across the 5 recording blocks. While this suggests that no confounding order effects influence the values over time, the precision estimates provided by the group and within-participant standard deviation quantify the amount of change expected from simply repeating the measure. Because these values incorporate both methodological and physiological change, they offer insight into the size of treatment effects that would be required to exceed this variance. Further research is required to explore the size of clinically relevant modifications of submental MEPs to simplify the process of determining participant sample sizes for researchers aiming to document the effects of treatments.

Objective determination of onset latency could not be achieved due to pre-MEP stimulus artefact. This artefact has been reported in another study of submental muscles, despite their use of an artefact-suppressing amplifier (Sowman, et al., 2009), suggesting susceptibility of MEPs recorded for this location to such artefact. This may relate to proximity of the recording electrodes, leads, or peripheral nerves innervating these muscles to the stimulating coil. Because this artefact prevented objective methods from being examined, all reported methods are subjective. This raises concern for researcher bias and/or error influencing findings. The current study of reliability of amplitude/area and onset latency values across five sessions involved measures by one rater only. To further investigate this issue, the inter-rater reliability of all methods should also be investigated. This would elucidate if any subjective preferences in the current study influenced the variance measures for each method.

This study shows that good (Portney & Watkins, 2009) reliability of onset latency values can be acquired from ensemble waveforms and the mean value of multiple MEPs. All amplitude/area methods achieved good (Portney & Watkins, 2009) reliability, and despite significant differences between most of them, all were highly correlated and demonstrated similar levels of precision. This suggests that although values may differ according to the method used, they all vary in a similar fashion. An accepted rationale for utilizing a rectified waveform, or obtaining mean latency and amplitude values from individual MEPs, over other methods is phase cancellation. While the current results cannot draw conclusions regarding how accuracy of measurement is diminished by the other methods, it has shown that the precision and reliability of measurement is not. In fact, rectification appears to give the least reliable estimate of latency under the conditions assessed in the present study. The distinction

between accuracy, reliability, and precision is crucial in this context. The current results of reliability and precision do not suggest which method is most accurate, and therefore research aimed at documenting such values should not employ methods which alter true amplitudes/area and latency values. If changes in MEP values across repeated-measures are of interest, the current study supports the contention of Sandbrink (2008, p. 254) that differences between various methods of data extraction are likely to be “minor” provided that the extraction method is consistent across assessments.



## Chapter 8: Pharyngeal pressures during swallowing within and across three sessions: within-subject variance and order effects<sup>19</sup>

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### 8.1 Introduction

Pharyngeal manometry is frequently used to document the immediate pressure changes associated with various swallowing techniques. Studies have compared pressures generated during both dry and manoeuvre swallows in healthy (Bulow, et al., 1999; Huckabee, et al., 2005; Huckabee & Steele, 2006; Pouderoux & Kahrilas, 1995; Witte, et al., 2008) and dysphagic participants (Bulow, et al., 2001; Lazarus, et al., 2002). For these studies, it is assumed that within-session measures are reliable and repeatable provided various manoeuvre swallows are counterbalanced and catheter placement remains stable throughout the session.

Conversely, the reliability or precision of measures obtained over separate sessions is not known. One study has reported acquisition of pressure values over two sessions but the researchers normalized the data to account for potential intersession variability (Huckabee & Steele, 2006). Intersession variability could potentially result from discrepancies in catheter position in the pharynx from placement to placement. A study designed to assess the position of a pharyngeal manometric catheter in the pharynx, when placed in one naris and then the other, found the catheter to sit at midline for both placements in only 1 of 10 participants (Doeltgen et al., 2007). Furthermore, this study found that in some cases, lateral position of the catheter is dependent on the naris in which the catheter is inserted.

Treatment studies that utilize pharyngeal manometry as a measure to document changes in pharyngeal pressure require assurance of measurement stability to attribute any changes in pharyngeal pressure measurements to treatment. No studies have investigated the variation in pharyngeal measures that results from simply removing and replacing a manometric catheter in a participant's pharynx.

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<sup>19</sup> **Macrae, P.**, Myall, D., Jones, R., & Huckabee, M-L. (2011). Pharyngeal pressures during swallowing within and across 3 sessions: within-subject variance and order effects. *Dysphagia*. (Online, DOI: 10.1007/s00455-010-9324-y).

The aim of this study was to document the variation in manometric measures of pharyngeal pressures across swallows within the same session and across three sessions. These data provide information on the variance introduced into pharyngeal pressure measures as a function of catheter placement, thus allowing for elucidation of treatment effects from methodological error in rehabilitation studies using normal participants, and a reference by which to evaluate the variance in dysphagic participants.

## **8.2 Method**

### **8.2.1 Participants**

Twenty healthy participants (gender equally represented, 18 – 35 years) were recruited for this study. They reported no history of dysphagia or neurological impairment. Ethical approval was obtained from the local institutional review board. Informed consent was obtained prior to commencement of data collection.

### **8.2.2 Instrumentation**

A 100-cm-long round catheter, 2.1 mm in diameter (Model CTS3 + EMG, Gaeltec, Hackensack, NJ), was used for manometric data collection. The catheter houses three solid-state, unidirectional, posteriorly-oriented sensors (2 x 5 mm) spaced 20 mm between sensors 1 and 2 and 30 mm between sensors 2 and 3 (as recommended by Salassa, et al., 1998). Data were collected using the Kay Elemetrics Digital Swallowing Workstation. Digitized 12-bit samples were obtained with a sampling frequency of 500 Hz and displayed in a -100 to 500-mmHg display window. The system software generates pressure waveforms as a function of time. The catheter was calibrated at 250 mmHg at room temperature. All measurements were displayed on a computer monitor during data collection and digitally recorded for offline analysis.

### **8.2.3 Procedures**

Participants were seated upright in a dental chair. Each participant completed three sessions, with a wide range of intersession intervals (30 min – 7 days) to minimize possible bias introduced by a single fixed interval. For session 1, the lubricated intraluminal catheter was inserted into one naris. Once the tip of the catheter reached the upper pharynx, identified by resistance at the posterior pharyngeal wall, the participant ingested water rapidly through a

straw until the catheter was pulled down approximately 35 cm into the proximal esophagus. The catheter was then pulled back out at increments of 10 mm, until high pressure in sensor 1, the uppermost sensor, suggested placement in the high pressure zone of the cricopharyngeus muscle (Castell & Castell, 1993). Pull-through was then done in 5 mm increments, requiring the participant to sit stationary, and dry swallow once after a period of approximately 30 s at each increment. Pull-through was continued until correct catheter placement was confirmed through visualization of the typical 'M' wave displayed at sensor 3 during swallowing (Castell & Castell, 1993). Standardization of catheter placement using the M wave has been documented in numerous studies (Gumbley, et al., 2008; Huckabee, et al., 2005; Huckabee & Steele, 2006; Witte, et al., 2008). Presence of the M wave indicates placement of the third sensor at the proximal border of the high pressure zone of the cricopharyngeus muscle (Castell & Castell, 1993). UES measures made with manometry sensor placement in this position have been documented to most closely reflect UES measures made using videofluoroscopy (Kahrilas, Dodds, Dent, Logemann, & Shaker, 1988). Sensors were oriented towards the posterior pharyngeal wall (Huckabee, et al., 2005; Huckabee & Steele, 2006) as confirmed by continuous monitoring of unidirectional markers on the catheter. The catheter was then secured to the nose with medical tape. Sensor 1 was therefore located in the oropharynx (approximately even with the base of the tongue), sensor 2 in the oropharynx (approximately even with the laryngeal additus), and sensor 3 in the proximal aspect of the tonically contracted upper esophageal sphincter (Curtis, Cruess, & Dachman, 1985). The distance from the third sensor to the nose tip for session 1 was noted. For sessions 2 and 3, the catheter was inserted into the same naris, and to the same distance in mm from the tip of the nose as was determined optimal in session 1. Participants executed five dry swallows and five 10 mL water bolus swallows in each session. A 10 mL water bolus was chosen to provide a contrast in volume to that of saliva swallows, which can be as much as 2 mL (Rudney, et al., 1995). There is also evidence to suggest that bolus volume may reach up to 10-12 mL during natural drinking situations (Bennett, Van Lieshout, Pelletier, & Steele, 2009). Participants were prompted to swallow whenever they felt comfortable, following a 30 s rest period. Participants were seated so they were unable to view the waveforms displayed on the computer monitor.

### 8.2.4 Data analysis

Peak or nadir pressures for each sensor were obtained offline. These were defined as the highest (sensors 1 and 2) or lowest (sensor 3) recorded pressure during each swallowing event. Due to the open cavity formation of the pharynx, contact pressure recordings were relative to atmospheric pressure. As one of the two conditions evaluated in this study did not involve ingestion of a bolus and as simultaneous fluoroscopy was not performed, pressure measurements reflected contact pressure rather than intrabolus pressure. Contact pressure represents convergence of the pharyngeal walls or the functional peristaltic wave of the pharynx, rather than intrabolus pressure (Brasseur & Dodds, 1991).

### 8.2.5 Statistical analysis

Using the R statistical analysis environment (R Development Core Team, 2010), linear mixed-effects models (Gelman & Hill, 2007; Pinheiro & Bates, 2000) were used to estimate the order effects and variability of the measures (both between sessions and within a session). To model amplitude, there were fixed effects of trial and session. The intercept, effect of trial, and effect of session were allowed to vary between participants. Confidence intervals were calculated for both the order effects and the variability to indicate the degree of uncertainty in the estimation of the parameters.

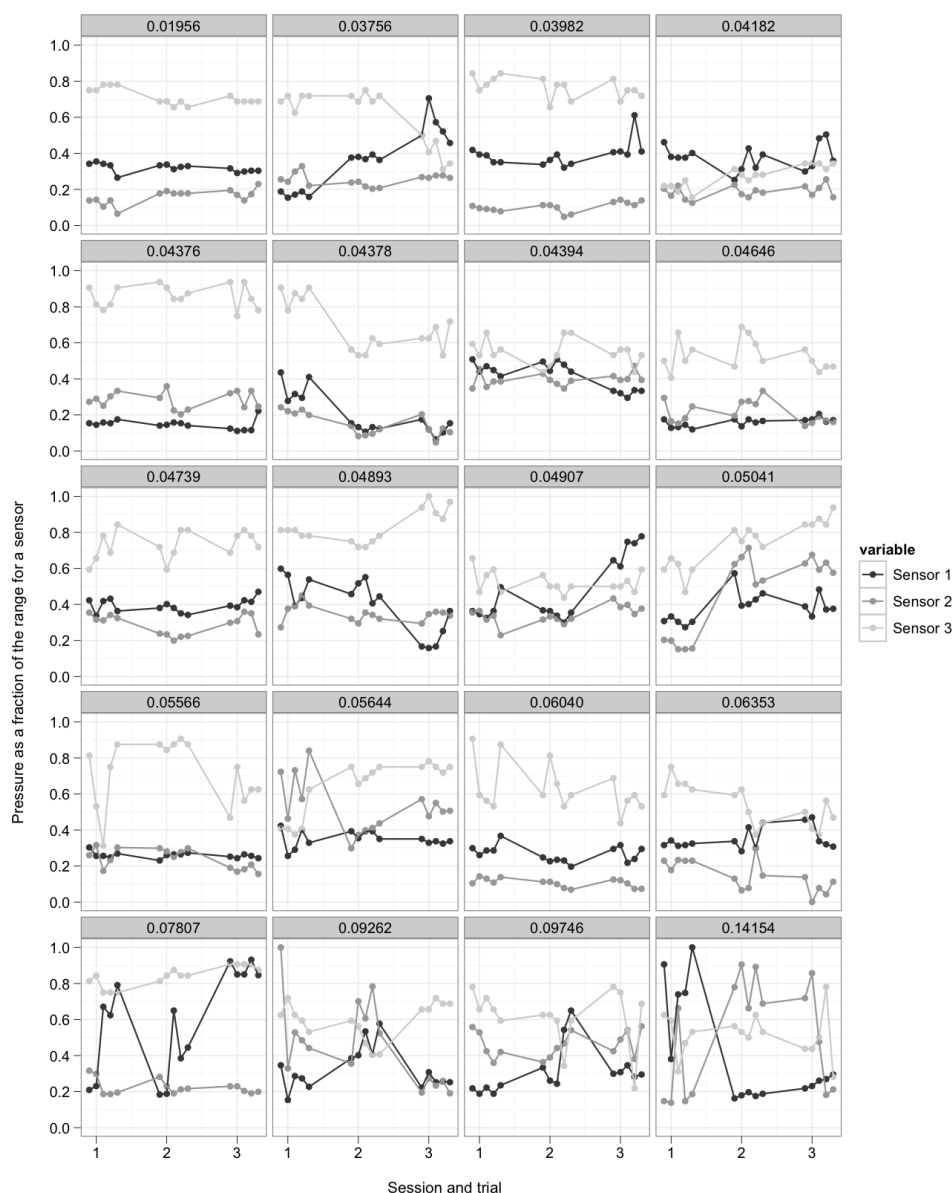
## 8.3 Results

Figure 8.1 displays raw data values for all 20 participants for each of the five trials plotted across each session for all three sensors for dry swallows only, as dry swallows are representative of both swallow types. Estimated baseline pressures (in mmHg with 95% confidence intervals) for dry swallows were 95 (77 – 113), 114 (93 – 136), and -13 (-16 – -10) for sensors 1, 2 and 3 respectively, and 91 (70 – 112), 112 (90 – 133), and -8 (-11 – -5) for 10 mL swallows.

The variability within and across sessions is shown in Table 8.1 as standard deviations with 95% confidence intervals, derived from the modelled data. Variability is greater across sessions than within sessions for sensors 1 and 2 during both dry and 10 mL swallows, as evidenced by the fact that the confidence intervals for both within- and across-session standard deviations do not overlap (albeit a slight overlap for sensor 2 during 10 mL



swallows), with larger across-session standard deviations. The across-session variance measured at sensor 3 is relatively comparable to that measured within sessions, as evidenced by overlapping confidence intervals for both and similar standard deviation estimates.



*Figure 8.1. Individual values for each of the five dry swallow trials at each sensor for sessions 1, 2, and 3, and for all 20 participants. Values have been normalized to the range of values at each sensor, for each condition, to make each value a percentage of the range. Each plot is titled with the individual mean of within-session variance, and progresses from least variable to most variable.*

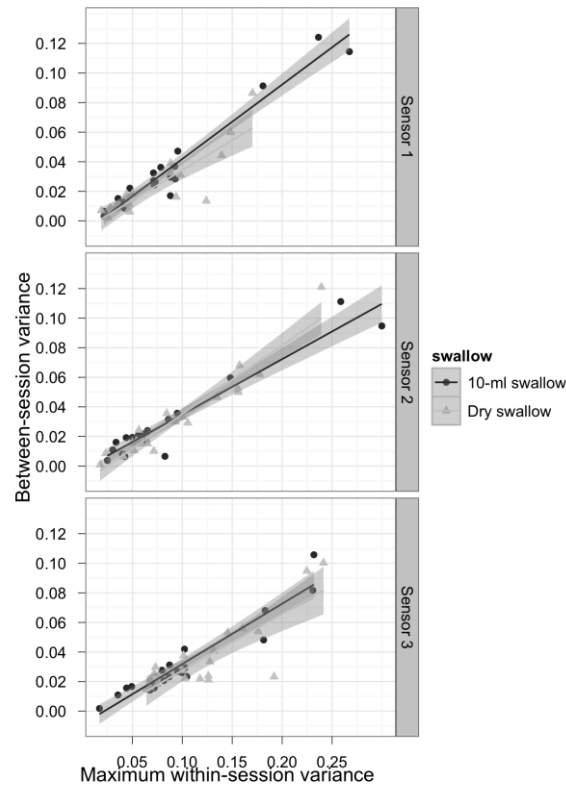
There was no evidence of a trial or session effect at any of the sensors for both dry and 10 mL swallows at the alpha level of 0.05. This is evidenced by the 95% confidence intervals around the estimates of change per trial and session in Table 8.1, all of which include zero (Colegrave

& Ruxton, 2003). The upper limits of the intervals suggest the estimated maximum change is no larger than 5% for trial and no larger than 12% for session (see Table 8.1).

To examine the relationship between within-session and across-session variability, correlations of the two were completed (Figure 8.2). Individuals' maximum within-session variance was plotted against the standard deviation for the three sessions for that individual. The two were highly correlated ( $r = .92$ ,  $p < 0.0001$ ), with no difference between the correlations for any of the three sensors.

**Table 8.1. Within- and across-session variability in pharyngeal pressures along with estimated order effects for pharyngeal pressures. Estimated values are shown with 95% confidence intervals (in brackets).**

Swallow	Sensor	Estimated change		Estimated change	
		SD across trials (mmHg)	per trial (mmHg)	SD across sessions (mmHg)	per session (mmHg)
Dry	1	13.4 (12.2 – 14.8)	0.4 (-1.2 – 2.0)	18.5 (14.5 – 23.7)	1.0 (-5.2 – 7.2)
Dry	2	17.3 (15.8 – 18.9)	-0.5 (-1.9 – 0.9)	27.5 (21.7 – 35.0)	-1.0 (-10.1 – 8.2)
Dry	3	3.0 (2.8 – 3.3)	-0.1 (-0.5 – 0.2)	3.6 (2.8 – 4.7)	-0.3 (-1.5 – 1.0)
10 mL	1	16.3 (14.8 – 17.9)	1.6 (-0.5 – 3.6)	29.4 (23.2 – 37.2)	1.2 (-8.5 – 10.9) <sup>††</sup>
10 mL	2	17.7 (16.1 – 19.5)	-1.6 (-3.3 – 0.1)	23.2 (18.1 – 29.8)	-0.1 (-7.9 – 7.8)
10 mL	3	2.6 (2.4 – 2.9)	-0.1 (-0.4 – 0.1) <sup>†</sup>	2.8 (2.2 – 3.7)	-0.1 (-1.1 – 0.8)
<sup>†</sup> Greatest change across trials (5%).			<sup>††</sup> Greatest change across sessions (12%).		



*Figure 8.2. Scatterplots of the relationship between within- and across-session variability for sensors 1, 2, and 3. Within-session variability reflects the largest individual within-session standard deviation. Across-session variability is the standard deviation of the mean of the three sessions.*

## 8.4 Discussion

This methodological study is the first to have determined the within- and across-session variability of pharyngeal contact pressure recordings during swallowing in normal subjects. This information is important to the emergence of manometry as a viable measure of change in rehabilitation research. The data presented here represent group variance for pharyngeal pressures during normal swallowing physiology, and have relevance in interpreting normative data of pharyngeal pressures provided by previous studies. Documenting this variance is important for studies using healthy participants which investigate changes in pharyngeal function as a result of swallowing manoeuvres. These data are also important for formulating power calculations for such studies, and for providing a reference by which to compare dysphagic pharyngeal pressure variation. These data suggest that peak and nadir pressures change less than 2% due to order effects, with the estimated maximal change not likely more than 5% in consecutive trials, and not more than 12% in consecutive sessions. The data also suggest that for sensor 1 and 2, variability is greater across sessions than within sessions, as

evidenced by the larger standard deviations for across-session values. Given the increased variability across sessions as compared with within a session, these data are important to consider when using manometry for repeated measures to document change as a result of treatments. The within-session variance documented here may also be useful for studies wishing to compare the pressure generation associated with different swallow techniques in the same session. As intrabolus pressure was not measured, the present findings are applicable to contact pressure only.

The present study used a 2.1 mm diameter round catheter housing unidirectional sensors. As evidence of radial asymmetry (McConnel, et al., 1991; Sears, et al., 1991) and advantages of an ovoid catheter in negating the problems with these asymmetries have been reported (Castell & Castell, 1993; Salassa, et al., 1998), there may be limitations associated with the manometry assembly used here. However, previous studies using the same catheter assembly as the present study have shown consistent measures of pharyngeal pressure (Butler, et al., 2009). Furthermore, the present study highlights that by maintaining sensors in a posterior orientation, pressures within the UES are relatively stable within and across sessions, with no significant order effects and an estimated maximum change of no more than 5% across trials, and 12% across sessions for all sensors. There is, however, reasonable variance in pressures measured at all sensors. Comparing the variance seen in the present study with that documented using circumferential sensors would provide insight into how different catheter placements is affected by radial asymmetry in the pharynx.

This study did not assess a range of bolus sizes, using only a 10 mL water bolus. Sensor 3, where the lumen surrounding the catheter is much smaller than in the pharynx, is more likely to be influenced by the presence of a bolus. However, within- and across-session variance was comparable across all sensors, for both dry and 10 mL water swallows. Comparing the variation within and across sessions documented in the present study with future studies using circumferential sensors and various bolus sizes would be of interest.

The variance within and across sessions depicted in Figure 8.1 shows a larger variation of values for some sessions than others, and some sensors more than others within individuals. In order to provide empirical evidence for dysphagia treatment techniques, measures need to be sensitive to changes in various swallowing parameters. The considerable within- and

across-session variability documented in this study suggests that attempts to validate treatments using pharyngeal manometry require either substantial effect sizes and/or participant numbers. The estimated variance across sessions shown in Table 8.1 ranges between 20% - 35% from the means across sessions for the different sensors and swallow types. With sufficient participant numbers, effects of smaller magnitude can be revealed, however, the clinical significance of such effects is questionable given that repeated measures in the absence of treatments induces change of this magnitude. If sources of variation can be identified and removed, the application of results from studies incorporating pharyngeal manometry should be improved.

Causes of variation across session may relate to changes in catheter placement from session to session. Doeltgen et al. (2007) evaluated variation in catheter placement using radiographic still images. In 5 of 10 participants, repeat catheter placement did not change catheter position in the pharynx. If their finding is applied to the present study, with 50% of participants showing varied catheter position in consecutive placements in the pharynx, our data suggest this variance will likely contribute to the increased variability seen in pressures across-sessions.

Variability within a participant could be influenced by individual anatomy. Anatomical variations could predispose measurements to the effects of catheter tolerance, or radial asymmetry. An interaction of differential catheter placement and anatomical differences may create more variation for one session and/or sensor compared with others, as seen in participant with mean within-session variance of 0.055 in Figure 8.1. Completing a similar investigation using radiographs would further elucidate the influence of catheter placement and anatomical differences on the variation within and across sessions.

The highly predictive relationship between within- and across-session variance (shown in Figure 8.2) suggests that utilizing individual means of pharyngeal pressures for a given session/sensor may not be the optimal first step in analysis of such data. If the goal of investigation is to reliably document change in swallowing pressures as a result of intervention, then assessing the within-session variability for individuals and excluding high variability sessions/sensors may result in more definitive results. While excluding data is typically not ideal in group analysis, and not generally possible in the assessment of patients,

it may be necessary for the purpose of effective treatment evaluation. Exclusion of data must be based on the inference that true values of pharyngeal pressure are not being recorded, so as to avoid bias. Figure 8.1 shows that while a given sensor may show substantial variability for a given session, other sessions show very reproducible values for the same sensor (see participant with mean within-session variance of 0.097, sensor 1, Figure 8.1). If high variability within sessions reflected true variation inherent in each individual swallow, all sessions should show similar variability for that sensor. By excluding highly variable units, it may be possible to increase the confidence that any change over sessions is small. For treatment studies, large confidence intervals increase the number of participants required to accurately determine the effect of a treatment.

Provided the variation reported in this study is considered in analysis of group treatment effects, pharyngeal pressure recorded using manometry can provide a valuable measure of change for treatment studies. Because this study did not assess pharyngeal pressures of patients with dysphagia, the values here must be considered to reflect normal swallowing physiology only. A meticulous approach to validation of dysphagia management techniques often involves initially documenting normal physiology (Logemann, 2005). Therefore, although these findings are not generalizable to the patient population *per se*, the data represent a first step in investigating variability in manometric measures of pharyngeal pressures. This data may serve as a reference for the variability seen in patient groups, and a basis for analysis of further studies of healthy participants. These data should also be considered in the interpretation of normative data for pharyngeal pressures. The large within- and across subject variability documented here suggest further studies in which this variability is eliminated are needed to gain a clear understanding of treatment effects on pharyngeal pressures before these treatments are applied to patients, where variability may be greater.

## Chapter 9: Discussion

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The methodological studies in this thesis assessed a combination of reliability, validity, and precision of four measures in an attempt to enhance current methods, and investigate alternative methods of measuring change in swallowing. While there are many measures available for swallowing research, evaluation of all instruments is beyond the scope of any one investigation.

Reliability assessments are particularly important for understanding the strengths and weaknesses of measures in swallowing research, where validity assessments are often unfeasible. While Chapter 5 investigated intra- and inter-rater reliability, the focus was to assess how reliability of using a reference point is influenced by rater-variance, and therefore the reliability of the entire process was not investigated. As no previous studies have assessed the reliability of data acquisition without the use of a reference point, the current study provides an alternative method of investigation, rather than enhancing the knowledge of existing methods. The advantage of the proposed method is that the need for complex data calibration and transformation is eliminated, therefore simplifying the process of assessing reliability, validity and precision of ultrasound as a measure of hyoid displacement. Future studies need to address the reliability of this method when participant variance is incorporated, as well as rater-variance across the entire process. Precision estimates are also required to determine the sensitivity of utilizing a reference point to treatment effects, therefore providing insight into the usefulness of this method in swallowing research and clinical evaluation. Alternatively, the study reported in Chapter 8 provided reliability estimates of the entire manometry process for healthy participants. This study is the first to have estimated the size of order effects associated with repeated manometry within and across sessions, thereby providing insight into its stability under the tested conditions.

The study in Chapter 8 differs to previous reliability studies by providing precision estimates of pharyngeal manometry both within and across sessions for healthy participants. While this study revealed no evidence of order effects, specification of within-participant variance across sessions provided insight into the amount of change expected in the absence of treatment. Previous literature has provided group standard deviations and, therefore, has only provided insight into variance at a group level and, therefore, the precision of within-participant repeated-measures was unknown. The specification of variance reported in Chapter 8 is useful

for designing future studies by providing insight into the sensitivity of pharyngeal manometry measures of healthy participants to treatment effects. Because no studies have documented the magnitude of cumulative treatment effects, or change considered clinically significant, it is not clear if manometry provides a responsive measure for such effects on pharyngeal pressures. However, the results from Chapter 8 show that within-participant treatment effects that are much smaller than 20% - 35% (depending on the sensor and swallow type of interest, see Section 8.4) would be negligible as they are substantially smaller than the change caused by repeating the technique alone. Chapter 7 also provides similar information by providing group and within-participant standard deviations across sessions. While this study was designed ultimately to compare the reliability and relationship between various methods of analysis, it also provides insight into change required from treatments of healthy participants to exceed variance arising from simply repeating the measure across five sessions. The comparison of the group variance estimates with the within-participant variance in Chapter 7 suggests that within-subject designs are more sensitive to treatment effects. However, as mentioned in Chapter 7, the within-participant precision estimates likely over-estimate the precision of repeated measures that occur on different days, when methodological variance is increased. The results from Chapter 7 and 8 prompt consideration of the precision of these measures when determining the magnitude of clinically relevant effects associated with treatment in future research. Research is now required to validate the responsiveness of both of these measures to cumulative treatment effects by firstly determining the magnitude of clinically significant effects in patient populations, and then assessing the responsiveness of these measures to such effects.

The use of MRI for quantifying CSA of the submental muscles detailed in Chapter 6 highlights the complexity of obtaining gold standard status for a measure. As MRI has been used to validate measures of limb muscles, but not the submental muscles specifically, it can only theoretically provide a comparison for ultrasound measures. However, the comparison of these two methods suggests advantages of ultrasound over MRI in quantifying these muscles. As the opposite has been reported for quantification of limb muscles, this reinforces the importance of context in interpreting validity and reliability assessments. Therefore, despite being unable to provide a true validity assessment of ultrasound, this research implies that developing the use ultrasound for quantifying CSA of swallowing muscles may be methodologically and finically easier than developing the use of MRI.



The four methodological chapters presented in Part II of this thesis aimed to provide ‘local evidence’ for some of the measures utilized for the treatment study presented in Part III of this thesis. As this information only provides a small contribution to that required in swallowing research, Table 9.1 was devised to provide a summary of available and required information for these methods. Red ticks represent information provided by Part II of this thesis. Black ticks represent information provided by previous studies.

**Table 9.1. Characteristics of swallowing measures.**

Ultrasound: Submental muscle morphometry					Ultrasound: Hyoid displacement					Manometry: Pharyngeal pressures					TMS: Corticomotor excitability				
r1	r2	V	P	Rs	r1	r2	V	P	Rs	r1	r2	V	P	Rs	r1	r2	V	P	Rs
✓ 20		✓		✓ 21						✓		✓ 22	✓	✓ 23	✓		✓ 24	✓	✓ 25

**r1 = intra-rater reliability, r2 = inter-rater reliability, V = validity, P = precision, Rs = responsiveness**

The attributes covered in this table are a small proportion of requirements for determining reliability, precision, validity, and responsiveness of these measures. Strictly speaking, as these factors change according to the tested population, all characteristics need to be defined for every cause of dysphagia, as well as different age groups, an immense task that could be considered unfeasible. Additionally, while intra- and inter-rater reliability is often reported, it often does not reflect reliability of the entire process, but rather the reliability of data analysis only, and therefore excluding some participant variance. While Chapter 5 addresses intra- and inter-rater agreement of data analysis, this information is not informative to a researcher wanting to know the variance associated with the data acquisition process, or repeated

<sup>20</sup> Emshoff et al., (1999)

<sup>21</sup> Watkin et al., (2001)

<sup>22</sup> Pauloski et al., (2009)

<sup>23</sup> Huckabee et al., (2005), Huckabee & Steele (2006), Lazarus et al., (2002), Ohmae et al., (2000), Pouderoux & Kahrilas (1995).

<sup>24</sup> Fraser et al., (2002), Jefferson et al., (2009a), Mistry et al., (2007), Power et al., (2004).

<sup>25</sup> Doeltgen et al., (2010a), Ertekin et al., (2001b), Fraser et al., (2002), Fraser et al., (2003), Gow et al., (2004a), Gow et al., (2004b), Hamdy et al., (1997), Hamdy et al., (1998a), Jefferson et al., (2009a), Jefferson et al., (2009b), Khedr et al., (2008), Khedr et al., (2009), Mistry et al., (2006), Mistry et al., (2007), Power et al., (2004).

measures of this process. As the level of detail required to encompass all variables associated with such assessment would not fit on a single table, these characteristics are checked if reliability or validity of the entire acquisition and analysis process is reported. As clinical correlates of indirect measures may provide more information than validity assessments per se, validity has been checked if there is research associating changes in these measures with other swallowing functions. Additionally, if the measure has been used to document change associated with treatment, regardless of whether these changes are cumulative or immediate and regardless of whether or not these effects have been deemed 'clinically significant', responsiveness has been attributed. It is important to be mindful of the interactions between reliability, validity, precision, and responsiveness when weighing up the strengths and weaknesses of each technique. Where treatment effects have been used to demonstrate the responsiveness of a measure in the absence of precision estimates, the 'responsiveness' may not reflect sensitivity to clinically significant effects. As mentioned above, any size effect can be revealed with a sufficient participant sample, but the clinical relevance of such an effect needs to be determined by assessing such effects against variance and functional outcomes. As Table 9.1 suggests, there is still a significant amount of research required to strengthen these few measures. By addressing the various missing components over time, swallowing research can provide increasingly robust results and direction for the management of dysphagia.

**PART III: EFFECTS OF NEUROMUSCULAR  
EXERCISE ON SWALLOWING  
BIOMECHANICS AND CORTICOBULBAR  
FUNCTION**



### 10.1 Introduction

The rapid succession of numerous biomechanical events necessary for effective passageway of the bolus from the mouth to the stomach leaves little room for error in the coordination of swallowing physiology. Minimal disruption to the timing or magnitude of any swallowing component can be detrimental to an individual's ability to maintain nutrition and hydration through oral intake (see Section 2.4.3 for more information on the pathophysiology of dysphagia). Dysphagia is associated with increased length of hospital stay, disability, death, and institutional care (Smithard, et al., 1996). The consequential effects of aspiration pneumonia, malnutrition, dehydration, and reduced quality of life complicate recovery in a substantial proportion of patients (Kind, et al., 2007; Langmore, et al., 1998; Nguyen, et al., 2005; Upadya, et al., 2004) (see Section 2.4.2 for more information on the consequences of dysphagia). Because dysphagia is a symptom of many different disorders, it interferes with the recovery period for patients following events such as traumatic brain injury and stroke, and confounds the progression of degenerative disorders such as Huntington's and Parkinson's disease (see Section 2.4.1 for more information on causes of dysphagia).

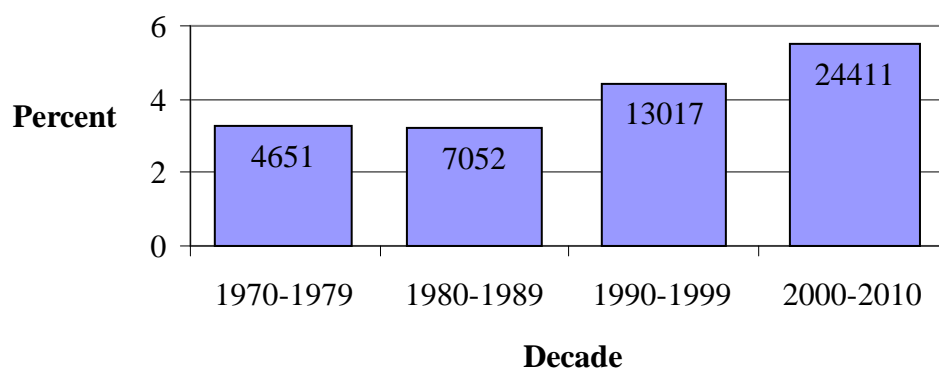
Rehabilitative techniques have been developed to address disorders of swallowing. The urgency to treat patients identified with dysphagia has historically provided the motivating force for the recommendation of treatment techniques. Thus, these techniques have emerged into clinical practice ahead of supportive, empirical evidence for application (Langmore, 1995; Robbins, et al., 2008; Rosenbek, 1995). The complexity of swallowing renders it difficult to implement research methods thorough enough to document all modifications that take place in the swallowing process as a result of therapy. A series of literature searches was conducted on PubMed search engine to assess the percentage of research articles containing the search-terms 'swallowing OR dysphagia' that also contained the term 'rehabilitation' across four decades. Figure 10.1 represents the percentage for each decade from 1970 – 2010. This shows that investigations with a focus of rehabilitation make up a relatively small

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<sup>26</sup> Sections of this chapter have been published in the following book chapter: Huckabee, ML., Macrae, PM. (accepted, 12.10, in press): Management and Treatment of Oropharyngeal Dysphagia – Adult: Rehabilitative Maneuvers and Exercise: Effortful Swallow. In: Manual of Diagnostic and Therapeutic Techniques for Disorders of Deglutition. Shaker, R., Postma, G., Belafsky, P., Easterling, C. San Diego: Springer.

proportion of swallowing literature. Consequently the effect of rehabilitation techniques on numerous swallowing parameters is still unclear.

Most of the available swallowing rehabilitation literature has investigated the biomechanical changes associated with treatment techniques (Bulow, et al., 1999, 2001; Easterling, Grande, Kern, Sears, & Shaker, 2005; Hind, Nicosia, Roecker, Carnes, & Robbins, 2001; Shaker, et al., 2002; Shaker, et al., 1997). Additionally, many research investigations document biomechanical changes at the time of executing techniques (Doeltgen, et al., 2009b; Huckabee, et al., 2005; Lazarus, et al., 2002), with very few studies providing evidence of cumulative treatment effects on regular swallowing (Easterling, 2008; Easterling, et al., 2005; Logemann et al., 2009; Shaker, et al., 2002; Shaker, et al., 1997). No studies have investigated the rehabilitative potential of effortful-swallowing as an isolated exercise protocol, therefore the literature reported here is based on the immediate effects documented during execution of the technique rather than its influence on non-effortful swallows. The cumulative effects of head-lift manoeuvre have been investigated by a small number of studies, allowing some assessment of its rehabilitative potential from reviewing this research.



*Figure 10.1. Percentage of published articles containing 'swallowing OR dysphagia' search-terms that also incorporate 'rehabilitation' search-term for each decade from 1970 – 2010. The total number of records containing 'swallowing OR dysphagia' are displayed inside each percentage bar.*

A number of techniques have been proposed and implemented for the rehabilitation of swallowing. These techniques include the head-lift (Shaker, et al., 1997) and Mendelsohn manoeuvre (Logemann & Kahrilas, 1990), designed to facilitate UES opening, the Masako manoeuvre, formulated to increase base of tongue to pharyngeal wall contact (Fujiu, 1996), and the effortful-swallowing technique, devised to increase laryngeal elevation and

pharyngeal contraction (see Huckabee & Pelletier, 1999 for review). Section 2.4.3 discusses the common impairments associated with dysphagia. The need for empirical evidence of the effects of treatment techniques aimed at remediating pharyngeal phase dysphagia forms the basis for the investigation of this treatment study. This review of the literature will address the head-lift manoeuvre and effortful-swallowing technique. These techniques are both neuromuscular exercises that aim to strengthen components of the pharyngeal swallow response. The choice of these techniques for comparison is based on the fact that both aim to increase muscular strength but differ in that, unlike head-lift manoeuvre, effortful-swallowing is executed in the context of swallowing. The reader is referred to Huckabee and Pelletier (1999) for an in-depth description of clinical application of these techniques to physiologic abnormalities of swallowing. Effortful-swallowing and head-lift manoeuvre are frequently recommended for treatment of acquired swallowing disorders following stroke or other neurological insult (Bulow, et al., 2001). The effects of both effortful-swallowing and head-lift manoeuvre on various swallowing parameters are detailed below.

## **10.2 The effortful swallow**

The effortful swallow technique was originally proposed as a compensatory manoeuvre, but is now widely accepted as a rehabilitation exercise for swallowing disorders (see Huckabee & Pelletier, 1999 for review). The change in application of effortful-swallowing from a compensatory to a rehabilitative technique results from the thought that muscle weakness can be reversed with exercise. The technique requires the patient to ‘swallow hard’, maximizing oral and pharyngeal muscle activation to achieve greater pressure on the descending bolus (Hind, et al., 2001), and encourages conscious control over oropharyngeal components of the swallow. Studies have documented changes in swallowing parameters that occur during execution of effortful-swallowing in healthy young (Huckabee, et al., 2005), healthy elderly (Hind, et al., 2001), and dysphagic (Bulow, et al., 2001) participants.

### **10.2.1 Effects of effortful-swallowing on swallowing biomechanics**

Greater submental muscle activation has been documented with effortful-swallowing (Huckabee, et al., 2005; Wheeler-Hegland, et al., 2008). The increase in sEMG measures during effortful-swallowing has implications for a number of biomechanical events including UES pressures and airway protection. A greater activation of submental musculature resulting in greater anterior and/or superior excursion of the larynx could be presumed to indirectly

influence closure of the laryngeal vestibule. Submental muscle activation is the driving force for hyolaryngeal excursion and, therefore, indirectly UES opening by powering the mechanical pulling force of the hyoid bone on the UES.

The observation that the duration of laryngeal closure increases with effortful-swallowing fits with the assumption that airway protection is facilitated by effortful-swallowing (Hind, et al., 2001; Ohmae, Sugiura, & Matumura, 2000). Earlier onset of submental muscle activation is seen during effortful-swallowing (Wheeler-Hegland, et al., 2008), and possibly explains the earlier onset of laryngeal and hyoid elevation prior to execution of an effortful swallow compared with a non-effortful swallow (Bulow, et al., 1999; Wheeler-Hegland, et al., 2008). However, while pre-swallow activation of the submental muscles appears to increase the amount of time the airway is protected, it doesn't seem to have the same influence on the magnitude of hyoid and laryngeal displacement. The findings for changes in extent of hyoid and laryngeal displacement vary slightly from study to study but reports of either unchanged (Wheeler-Hegland, et al., 2008) or decreased displacement (Bulow, et al., 1999; Hind, et al., 2001) is seen for effortful compared with non-effortful swallows. It is difficult to assess whether this decrease has negative implications for swallowing but assessing the results for other biomechanical aspects of swallowing may help in clarifying this issue. For example, a reduction in laryngeal displacement may result in less effective closure of the airway, despite increased duration of closure. However, effortful-swallowing has been shown to reduce the depth of penetration into the larynx and trachea (Bulow, et al., 2001), suggesting no compromise of laryngeal closure during execution of the technique.

A decrease in laryngeal displacement may also cause a decrease in UES opening but the width of UES at maximal opening is reportedly unchanged in the face of this decrease in displacement (Hind, et al., 2001). Furthermore, an increase in the magnitude of upper esophageal sphincter (UES) pressures (Huckabee, et al., 2005; Witte, et al., 2008), and relaxation duration (Hind, et al., 2001; Hiss & Huckabee, 2005; Ohmae, et al., 2000) has been documented during effortful-swallowing. Increased magnitude of UES nadir pressures represent decreased resistance to bolus transfer into the esophagus. An inverse relationship has been documented between hyoid excursion and nadir UES relaxation pressure (Jacob, Kahrilas, Logemann, Shah, & Ha, 1989), suggesting that greater magnitude of nadir pressures reflects greater "suction" created at the anterior portion of the UES by hyolaryngeal traction



(Jacob, et al., 1989, p. 1474). While the increase in sEMG documented with effortful-swallowing has been significantly and negatively correlated with UES pressures (Huckabee, et al., 2005), the correlation was low ( $r = -.179$ ). This suggests an increase in sEMG alone is insufficient to drive the lower UES pressures documented, and instead may be the result of a number of biomechanical changes associated with the technique. These findings suggest that effortful-swallowing assists with UES opening during swallowing (Witte, et al., 2008), resulting in more favourable pressures for bolus transfer.

### ***10.2.1.1 Pharyngeal pressures***

Despite the positive modifications on swallowing biomechanics documented during effortful-swallowing, there are discrepancies in the literature regarding how these changes affect pharyngeal pressures. The discrepancies raise questions about both the rehabilitative and compensatory application of effortful-swallowing for heterogeneous populations.

There are many biomechanical events that contribute to pharyngeal pressures, including: pharyngeal and oral muscle contraction; closure of the larynx, lips and velopharyngeal port; and tongue movement (Perlman & Christensen, 1997). These actions together are responsible for bolus propulsion and effective bolus clearance (Miller, 1999; Perlman & Christensen, 1997). When reporting the effects of effortful-swallowing on healthy participants, various studies using manometry to quantify peak and nadir pressures in the pharynx have documented a significant increase in pharyngeal pressures (Huckabee, et al., 2005; Huckabee & Steele, 2006; Ohmae, et al., 2000) and pharyngeal pressure duration (Bulow, et al., 1999; Hind, et al., 2001; Hiss & Huckabee, 2005; Ohmae, et al., 2000; Steele & Huckabee, 2007; Witte, et al., 2008). These findings suggest effortful-swallowing is effective for treating dysphagia resulting from decreased bolus propulsion and clearance. However, as there are mechanisms other than pharyngeal muscle contraction that may be impaired in the case of decreased pharyngeal pressure, more information is needed about which of these mechanisms are influenced by effortful-swallowing.

Tongue movement is presumably greater during effortful-swallowing, based on findings of increased oral pressures with effortful-swallowing (Hind, et al., 2001; Lever et al., 2007). The finding that anterior bulging of the posterior pharyngeal wall decreases with effortful-swallowing, but base of tongue to posterior pharyngeal wall contact pressure increases

(Ohmae, et al., 2000) implies that increases in pharyngeal pressure at the level of the base of tongue in healthy (Ohmae, et al., 2000; Pouderoux & Kahrilas, 1995) and dysphagic participants (Lazarus, et al., 2002) is also likely to result from altered tongue movement during the effortful-swallowing.

Early studies into the effects of effortful-swallowing on pharyngeal pressures by Bulow and colleagues report findings that have been contradicted in later investigations (Huckabee, et al., 2005; Huckabee & Steele, 2006). Bulow and colleagues found no significant pressure or duration of pressure differences in the pharynx and UES when effortful were compared with non-effortful swallows (Bulow, et al., 1999, 2001). Although no findings reached significance, suggesting no differences between the two conditions, trends of decreased pressure at the level of the inferior constrictor during effortful-swallowing were reported for both dysphagic (Bulow, et al., 2001) and healthy participants (Bulow, et al., 1999). This finding raises questions regarding the use of this technique for the purpose of enhancing bolus propulsion and clearance.

The studies by Bulow and colleagues (1999, 2001) also show a trend for decreased magnitude of UES nadir pressures during effortful swallows, suggesting the technique may result in greater resistance for the bolus in the transfer from pharynx to esophagus, or less hyolaryngeal traction (Jacob, et al., 1989). For dysphagic patients, a trend towards decreased duration of UES relaxation was also documented for effortful swallows (Bulow, et al., 2001), with the opposite seen for healthy participants (Bulow, et al., 1999), suggesting some differences in the way healthy and disordered systems respond to the technique. Given that other studies of healthy participants have also found increases in UES relaxation duration (Hind, et al., 2001; Hiss & Huckabee, 2005), this seems a plausible explanation. However, many trends reported in the Bulow study of healthy participants (Bulow, et al., 1999) are in contrast to other studies of healthy participants (Huckabee, et al., 2005; Huckabee & Steele, 2006), suggesting clarification of the discrepancies is essential before drawing conclusions about the application of effortful-swallowing in dysphagia management. Furthermore, as the technique potentially results in negative effects on swallowing biomechanics, clarification is essential to avoid exacerbation of physiologic deficits.

A consideration when comparing the Bulow studies to those with conflicting findings is the statistical power achieved. While studies to date haven't typically reported power statistics, the larger number of participants and trials utilized in the Huckabee studies may contribute to the different findings reported to those completed by Bulow and colleagues. As studies with similar participant numbers and trials have also rendered conflicting findings alternative factors that differ between studies also warrant consideration.

### **Possible explanations for discrepancies in the literature regarding the effects of effortful-swallowing on pharyngeal pressures**

Varied instructions on how an effortful swallow is to be executed may contribute to these discrepancies (Huckabee, et al., 2005). An effortful swallow is typically completed following the instruction to 'swallow hard', but the emphasis on whether tongue or pharyngeal muscles should be maximally contracted may change the observed effects on pharyngeal pressures (Huckabee & Steele, 2006; Steele & Huckabee, 2007). The observation that similar instructions have yielded dissimilar results suggests this variable alone is unlikely to explain the contrasting findings (Bulow, et al., 1999, 2001; Huckabee, et al., 2005; Huckabee & Steele, 2006; Witte, et al., 2008).

The use of a bolus during effortful-swallowing in studies may determine the differential effects on pharyngeal pressures reported (Witte, et al., 2008). Early investigations involved execution of the manoeuvre with a bolus (Bulow, et al., 1999, 2001; Bulow, Olsson, & Ekberg, 2002; Hind, et al., 2001; Lazarus, et al., 2002; Pouderoux, et al., 1995), while more recent studies utilized saliva swallows and reported some contrasting results to those reported previously (Hiss, et al., 2005; Huckabee, et al., 2005; Huckabee, et al., 2006; Steele, et al., 2007). To further investigate if the presence of a bolus could influence the findings, Witte et al. (2008) investigated the effect of effort on both saliva and 10 mL water boluses. They concluded that the effects on pharyngeal pressures are the same for both bolus and non-bolus conditions, with the exception of one significant difference. This study suggested a role of the bolus in decreasing the magnitude of UES nadir pressures measured with manometry. The study also added to the pool of conflicting findings, reporting no increase in pharyngeal pressures associated with effortful-swallowing, suggesting alternative confounds in studies to date.

Witte et al. (2008) suggested that the use of biofeedback during training of the technique as a possible cause of their conflicting findings to those found previously in the same laboratory (Huckabee, et al., 2005; Huckabee, et al., 2006). However, there are also contradictory findings from studies that have not used biofeedback in training the technique (Bulow, et al., 1999; Steele & Huckabee, 2007).

The differences in anatomic location of pharyngeal pressure measurement may also explain uncertainty around the effects of effortful-swallowing (Witte, et al., 2008). For the series of studies by Bulow and colleagues (Bulow, et al., 1999, 2001; Bulow, Olsson, & Ekberg, 2002), measurement was at the level of the lower pharynx only. Other studies have reported increased pressure (Lazarus, et al., 2002; Poudroux & Kahrilas, 1995) and increased duration of pressure generation (Lazarus, et al., 2002) at the level of the base of tongue for the technique. Although it is possible that pressure changes at the level of the base of tongue went undetected in the Bulow studies, their findings at the level of the lower pharynx still differed to other studies (Huckabee, et al., 2005; Huckabee & Steele, 2006), suggesting other sources of conflict.

There is a possibility that effortful-swallowing influences men and women differently. Witte et al. (2008) found that greater duration of pressure generation at the oropharynx occurred with non-effortful swallows for men, but with effortful swallows for women. Another study found no differences in gender responses to effortful-swallowing (Huckabee, et al., 2005). A study including a larger number of participants does not report gender effects; however this study does not state whether gender was equally represented, and so these effects may not have been analysed (Hind, et al., 2001). Other studies have included only one gender in the participant group (Huckabee & Steele, 2006; Steele & Huckabee, 2007), or not stated the gender of participants (Hiss & Huckabee, 2005), meaning gender differences cannot be ruled out as a possible cause for opposing results.

It is also possible that the effects of effortful-swallowing vary with age. Studies investigating the effects of the technique have used participant groups of varying ages. One study controlled for this variable and found pyriform sinus residual was greater in effortful swallows than in non-effortful for elderly participants, and the opposite in younger participants (Hind, et al., 2001).

### **10.2.2 Cumulative and lasting effects of effortful-swallowing**

The studies discussed thus far highlight the biomechanical modifications that take place during effortful-swallowing and provide valuable information about the compensatory possibilities of the technique; that is, what immediate changes in swallowing biomechanics occur during implementation. Three studies have looked at the lasting effects of effortful-swallowing and other techniques on swallowing biomechanics within the context of a clinical treatment paradigm. These studies have documented positive outcomes for dysphagic patients using the technique as part of a rehabilitation plan, including a decrease in aspiration-related pulmonary symptoms, removal of enteral feeding tubes and a return to full oral intake, increased activation of swallowing musculature and continued functional improvements in swallowing following termination of therapy (Bryant, 1991; Crary, 1995; Huckabee & Cannito, 1999). Although these findings suggest rehabilitative promise for the technique, the treatment protocols evaluated have all included additional exercises in conjunction with effortful-swallowing and, therefore, positive outcomes cannot necessarily be attributed to effortful-swallowing *per se*. The dose and frequency specified by these studies range from 10 one-hour sessions over five days (Huckabee & Cannito, 1999), to 10 weeks, with no details provided of the duration of sessions within this period (Bryant, 1991). All of these studies utilized VFS to document improvements in swallowing physiology. However, interpreting the specific physiological deficits that were influenced by the effortful-swallowing technique is unachievable due to the combination of treatments utilized, and the various physiologic impairments included in each study. While inclusion of various types of impairment is necessary to represent dysphagic populations, studies utilizing the effortful-swallowing technique as an isolated treatment exercise are required for more clarity into its cumulative effects on swallowing physiology. These studies have provided valuable direction for swallowing research by setting a precedent for investigating cumulative efficacy of treatment techniques.

### **10.2.3 Negative effects of effortful-swallowing**

Substantial nasal redirection has been reported during a rehabilitation programme that resolved once effortful-swallowing practice ceased (Garcia, Hakel, & Lazarus, 2004). After viewing videofluoroscopic images of the execution of the technique, the authors concluded that the timing of base of tongue contact with the posterior pharyngeal wall was altered, creating an obstruction to bolus flow in the upper pharynx. This obstruction prior to closure of

the velopharyngeal port resulted in nasal redirection on 100% of swallows. An alternative explanation is that compromised velopharyngeal closure may have been exacerbated with increased force of the pharyngeal musculature. With the various mechanisms available to patients to perceptively increase the 'strength' of a swallow, there are possibilities for incorrect execution to combine with physiologic impairment, resulting in aggravation of an existing problem, or initiation of a new one.

A study by Bulow and colleagues (2001) also reports a case in which severe pharyngeal dysfunction was exacerbated by effortful-swallowing. All participants were reported to have either severe or moderate pharyngeal dysfunction; however, the variable of underlying physiologic deficits causing the dysphagia was not controlled, making it difficult to determine the specific physiologic impairment aggravated by the technique. The findings of these two studies stress the need for an understanding of the effects of treatment techniques on various physiologic deficits.

Studies to date show some trends in how effortful-swallowing influences swallowing biomechanics. The fact that some effects have been shown to be sensitive to factors such as age and gender suggest further investigation needs to control factors of variance using a larger participant group in a single study. A participant group including mixed age and gender may help to elucidate the discrepancies in findings that have come from studies both across and within laboratories (Huckabee, et al., 2005; Huckabee & Steele, 2006; Witte, et al., 2008).

While predictions can be made based on the effects documented by these studies regarding biomechanical adaptations that occur during effortful-swallowing, more focussed research is required to isolate the specific cumulative effects of effortful-swallowing as a rehabilitation treatment.

### **10.3 The head-lift manoeuvre**

The head-lift manoeuvre is a relatively new exercise used in the rehabilitation of swallowing disorders. Like effortful-swallowing, the idea that the biomechanics of muscle weakness, seen in conditions such as sarcopenia (muscle weakness as a result of aging), can be reversed with muscle strengthening exercises (Karakelides & Nair, 2005) provides the basis for this technique.

The head-lift manoeuvre requires the participant to lie supine on a flat surface and lift the head to view his or her toes without lifting the shoulders (Shaker, et al., 1997). This lift is repeated 30 times, during which no hold is maintained at the peak of the lift (isokinetic portion). The lift is then repeated three times in a sustained manner in which the peak lift point is held for 1 min (isometric portion). The aim is to increase the strength of the mylohyoid, geniohyoid and the anterior belly of the digastric muscles (also known collectively as the submental or floor of mouth muscles), to create greater traction force from hyolaryngeal excursion to assist with opening of the UES (Ferdjallah, Wertsch, & Shaker, 2000; Shaker, et al., 2002). As the submental muscles are integral in airway protection through hyolaryngeal excursion, strengthening these muscles also presumably influences this biomechanical event.

### **10.3.1 Cumulative and lasting effects of head-lift manoeuvre on swallowing biomechanics**

Unlike effortful-swallowing, head-lift manoeuvre has been investigated as an isolated rehabilitation technique with lasting effects documented for swallowing biomechanics using videofluoroscopic evaluation of swallowing (VFS) following six weeks of the treatment for healthy participants (Easterling, 2008; Easterling, et al., 2005; Shaker, et al., 1997) and dysphagic patients (Logemann, et al., 2009; Shaker, et al., 2002). An increase in both anterior laryngeal excursion and UES opening is reported in healthy elderly participants (Easterling, et al., 2005; Shaker, et al., 1997) following the treatment protocol. While an increase in anterior *laryngeal* excursion has been documented after six weeks of the technique (Easterling, et al., 2005; Shaker, et al., 2002; Shaker, et al., 1997), only one study has documented an increase in anterior *hyoid* displacement (Easterling, et al., 2005). Additionally, three studies have failed to detect significant changes in *hyoid* displacement (Logemann, et al., 2009; Shaker, et al., 2002; Shaker, et al., 1997). As hyolaryngeal excursion is influenced by both hyoid and laryngeal displacement, the discrepancy in how these two structures are affected suggests muscle specific to each are differentially affected by the technique. Another study has found hypopharyngeal intrabolus pressure to decrease following treatment (Shaker, et al., 1997), which is known to signify less resistance for the descending bolus (Brasseur & Dodds, 1991). When Shaker et al. (2002) prescribed the same treatment plan for patients who were fed non-orally as a result of poor UES opening, they found similar results and a post-treatment return to full oral intake with no evidence of aspiration for any participant. Maximum

anteroposterior opening of the UES reportedly increases after six weeks of the exercise (Easterling, et al., 2005; Shaker, et al., 1997), however the duration of opening is not affected (Shaker, et al., 1997). Furthermore, while adaptations in UES opening are evident following the head-lift exercise (Logemann, et al., 2009; Shaker, et al., 2002), similar adaptations have been documented for a sham exercise group (Shaker, et al., 2002), and traditional therapy used as a control (Logemann, et al., 2009). While these studies suggest maximum opening of the UES may be facilitated, the results don't appear to be specific to the head-lift manoeuvre. It has been proposed that increased anteroposterior UES opening and anterior excursion of the larynx documented after six weeks of head-lift manoeuvre is due to an increase in submental muscle activation (Shaker, et al., 2002), however, this has not been explicitly demonstrated.

Implications of submental muscle strengthening following the head-lift manoeuvre have been made from fatigue analysis studies. Strengthening of the submental muscles is presumed based on the finding that these muscles demonstrate fatigue during the isometric head-lift (Ferdjallah, et al., 2000; Jurell, Shaker, Mazur, Haig, & Wertsch, 1997). Only one study has documented submental muscle fatigue before and after the head-lift exercise protocol for comparison of activation levels (White, Easterling, Roberts, Wertsch, & Shaker, 2008). This study concludes that *increased* fatigue resistance demonstrated in the sternocleidomastoid muscle indicates *increased* strength. Because the study documented *reduced* fatigue resistance in the submental muscles after six weeks of the exercise, the authors concluded that the initial stages of the exercise increase strength in the sternocleidomastoid muscle, after which the exercise load increases for the submental and infrahyoid muscles. This suggests that strengthening of the submental and infrahyoid muscles occurs following continued practice of the exercise, only once fatigue resistance is achieved in the sternocleidomastoid muscle (White, et al., 2008). Further research is required to document the translation of fatigue resistance to muscle strength, and to assess how muscle activation is influenced by the head-lift manoeuvre.

These studies suggest that physiological changes underlying swallowing take place with repetitive execution of head-lift manoeuvre. However, some limitations of this research have been raised and warrant consideration. Investigation of the effects of the treatment on dysphagic patients utilized a 'sham' treatment condition (Shaker, et al., 2002). However, the person responsible for subjective clinical assessment of swallowing function was not blinded



to the treatment each patient received. Furthermore, assignment of patients to the sham condition was terminated before recruitment was completed, with all patients subsequently assigned to receive the head-lift treatment. While randomization occurred for allocation of patients to the sham or treatment group initially, subjective assessment of secretion management by the enrolling researcher brought about the decision to terminate the sham condition (Shaker, et al., 2002, p. 1316). At the time the sham condition was terminated both the real-exercise and sham-exercise groups were evaluated for changes from their baseline measures. The study reports a significant increase in anteroposterior UES opening for the real-exercise but not the sham-exercise group. However, when a between-group statistical comparison was made, the two groups showed no difference in this measure. Increasing the data available for both groups would have provided more insight into whether this effect was specific to the head-lift exercise. As another study of the head-lift exercise has shown changes in anteroposterior UES opening in a control group (Logemann, et al., 2009), the possibility that continuing the sham condition may have resulted in different findings cannot be discounted.

More recent studies have extended the research on the head-lift manoeuvre to look at changes in other swallowing outcomes and other functions such as vocal quality (Easterling, 2008; Logemann, et al., 2009). The study by Easterling (2008) recruited 21 healthy older participants to the head-lift condition, and five healthy older controls who did not complete the exercise. While “significant improvement in deglutitive biomechanics” (page 321) was reported for half of the head-lift participants, a single *p*-value is reported for the three biomechanical measures, making it difficult to establish the differential response of these measures. However, pre- and post-exercise means and standard deviations suggest the magnitude of increase for the three biomechanical measures ranged from 1 – 2 mm. The results also indicate that improvements are sensitive to dose and frequency of therapy, with improvements documented only for participants who were able to attain the exercise goals. A large proportion of participants were unable to achieve goals of the exercise, reducing the original sample by 52%. A previous study by Easterling and colleagues (2005) found that only 68% of healthy participants were able to attain the isometric goal by week 5, raising concern for maintenance of participation based on attainment of goals (Easterling, et al., 2005). However, these studies (Easterling, 2008; Easterling, et al., 2005) are based on healthy

participants and therefore maintenance of exercise participation may not reflect that of dysphagic patients, for who benefits of exercise may provide a motivating factor.

A more recent study was conducted to assess the effects of head-lift manoeuvre on swallowing function of dysphagic patients of mixed aetiologies (Logemann, et al., 2009). Using more stringent methods of blinding, this study found no differences in hyoid, laryngeal, or UES parameters between the groups. The study did, however, report a decrease in *post-swallow* aspiration after six weeks of head-lift manoeuvre exercise. The traditional therapy group acting as a control for this study included the ‘supraglottic swallow’ technique which is designed to target aspiration that occurs *during* the swallow. Exclusion criteria for this study included aspiration *during* the swallow, possibly biasing the results towards a lack of change in aspiration measures for the traditional therapy group.

### **10.3.2 Muscle activation during execution of the head-lift manoeuvre**

Other studies have employed surface electromyography (sEMG) to document the level of muscle activity during the head-lift manoeuvre. These studies have verified the role of the suprahyoid muscles during the technique and have also provided evidence of activation in the infrahyoid muscles (including the sternothyroid, sternohyoid, thyrohyoid, and omohyoid) and the sternocleidomastoid muscle (Alfonso, Ferdjallah, Shaker, & Wertsch, 1998; Ferdjallah, et al., 2000; Jurell, et al., 1997; Mepani et al., 2009; White, et al., 2008). The results of these studies vary with regards to fatigue rates of the muscles involved. Ferdjallah (2000) found the sternocleidomastoid fatigued more rapidly than the infrahyoid or suprahyoid muscle group, and proposed that this may be a limiting factor of the exercise given the sternocleidomastoid does not play a role in swallowing. In contrast, two smaller investigations completed prior to Ferdjallah’s study found the infrahyoid and suprahyoid muscles fatigue at a faster rate, with less consistency of fatigue rates seen across participants for the sternocleidomastoid. Another recent study (White, et al., 2008) confirms this inconsistency but suggests that the sternocleidomastoid fatigues as fast as or faster than infrahyoid and suprahyoid muscles. Regardless of the limiting role the sternocleidomastoid may play, fatigue is registered in the suprahyoid and infrahyoid muscles immediately after initiation of the exercise (Ferdjallah, et al., 2000). A recent study assessing muscle fatigue over different durations of the isometric component of the head-lift found, surprisingly, that the muscle groups exerted more force for the 20 s hold than for the 60 s hold (White, et al., 2008). While the authors allowed 5 min rest

between each isometric contraction, unrandomized task order and cumulative fatigue that has been documented in the sternocleidomastoid (Ferdjallah, et al., 2000) may have influenced these results.

While studies on head-lift manoeuvre suggest that positive results can be seen following six weeks of the exercise, more research is required to provide clarification. Given the results of the studies above, the following issues need to be considered. The Easterling study (2008) proposed that the difficulty of technique execution resulted in participants decreasing the dose or frequency of exercise. This study also concluded that decreasing dose and frequency negatively influences the outcomes. Adapting the exercise to make the isometric portion more attainable may prevent participants from decreasing the frequency of exercise. However, this decrease in isometric intensity may also result in decreased effect of the technique on swallowing physiology. Considering the results of the muscle fatigue studies above, it appears fatigue begins immediately after isometric contraction begins (Ferdjallah, et al., 2000), and possibly to a greater extent over a 20 s period when compared with a 60 s period (White, et al., 2008). Reducing the duration of the isometric contraction to 30 s rather than 60 s may inhibit participant drop-out by making the goals of the exercise more attainable. While it has been shown that this reduction is likely to achieve similar therapeutic fatigue levels as a longer isometric contraction (White, et al., 2008), the lack of improvements for participants with reduced exercise attainment (Easterling, 2008) suggests it is possible that such a modification could have the opposite effect.

The inconclusive findings regarding hyolaryngeal excursion suggest more research is required to confirm biomechanical changes associated with the technique. As infrahyoid activation has been documented to the same level as suprahyoid muscles, negative effects on hyolaryngeal excursion could potentially result. Additionally, assessment of the influence of head-lift manoeuvre on other swallowing parameters is also necessary. Specific measurement of pharyngeal muscle contact pressure using manometry following this treatment would provide a clearer picture of what physiologic changes are responsible for the decrease in intrabolus pressure shown by Shaker et al. (1997).

## **10.4 Exercise characteristics that enhance recovery**

Motor recovery is reliant on repetition of exercise but the exercise characteristics that will promote optimal recovery vary depending on the target movement (Rose & Christina, 2006) and site of lesion (Renner, Schubert, Jahn, & Hummelsheim, 2009). It is known that there is a relationship between recovery of motor function, dendritic changes in the cortex and synaptic changes affecting neural transmission (Nudo, 2003, 2006), but how these phenomena can be positively influenced by behavioural treatments is not clearly understood (Keefe, 1995). The role of neural plasticity specific to swallowing recovery is even less clear (Robbins, et al., 2008). To hypothesize the impact that effortful-swallowing and the head-lift manoeuvre have on corticomotor function associated with swallowing, it is necessary to consider the components of each technique.

### **10.4.1 Skill versus strength training**

Effortful-swallowing achieves muscle strengthening by requiring increased effort for each repetition of the exercise, therefore necessitating active attention from the participant. Head-lift manoeuvre achieves muscle strengthening through isokinetic and isometric muscle contractions (Shaker, et al., 1997), without requiring conscious attention to the movements involved. Conscious effort or challenge during exercise creates a skill learning component for rehabilitation tasks. Effortful-swallowing is carried out in the context of swallowing function and is, therefore, a task-oriented exercise in that the technique replicates the desired task, i.e., swallowing. Effortful-swallowing can consequently be defined as a task-oriented form of skill training, with a strength component resulting from greater muscle activation than produced during regular swallowing (Burkhead, et al., 2007). In contrast, head-lift manoeuvre is a muscle strengthening exercise that targets muscles (submental) involved in one component of the swallowing process, i.e., hyolaryngeal excursion. Head-lift manoeuvre is consequently defined as a non-task-oriented form of strength training.

#### ***10.4.1.1 The effects of skill and strength training on functional motor performance***

The specificity of practice hypothesis put forward by Barnett and colleagues (1973) proposes that specific motor skills are developed and stored through practice, and that these motor skills do not generalize across tasks. This hypothesis would presume that the balance skills

required for standing on one leg do not utilize the balance skills required to successfully ride a bike; instead, both tasks utilize specific balance skills acquired through practice of the respective tasks. The importance of task-oriented exercise training has been documented in many research studies (Van Peppen et al., 2004) and is considered crucial to foster optimal motor learning (Richards et al., 1993). Following from this, it has been observed that functional outcomes for rehabilitation depend on how closely the specific exercise(s) replicates that task (Lindquist et al., 2007). This concept is supported with findings related to functional outcomes for standing (de Leon, Hodgson, Roy, & Edgerton, 1998b) and walking. Richards et al. (1993) found that total time engaged in specialized gait training, rather than total therapy time, positively influenced functional gait outcomes.

Further physiotherapy literature suggests that isolated strength training programmes fail to produce improvements in functional movement outcomes, despite increasing strength (Liu-Ambrose, Taunton, MacIntyre, McConkey, & Khan, 2003; Rasch & Morehouse, 1957; Remple, Bruneau, VandenBerg, Goertzen, & Kleim, 2001; Symons, Vandervoort, Rice, Overend, & Marsh, 2005; Van Peppen, et al., 2004). Furthermore, specificity of practice is seen for strength training with a lack of transfer of strength improvements observed for untrained tasks (Liu-Ambrose, et al., 2003; Rasch & Morehouse, 1957). One study has suggested isokinetic exercise of the ankle increases not only strength but also proprioception and functional movement (Sekir, Yildiz, Hazneci, Ors, & Aydin, 2007). However, this study used the same instrumentation for training and assessment tasks, signifying specificity of practice may in fact contribute to the differences documented by these authors.

#### ***10.4.1.2 The effects of skill and strength training on corticomotor function***

Improvements in motor function have been associated with plasticity of cortical regions such as the primary motor cortex and supplementary motor area (Aizawa, Inase, Mushiake, Shima, & Tanji, 1991). Changes in representation in the motor cortex have been shown to result from both spontaneous recovery of motor impairment (Hamdy, et al., 1998b) and functional movement training (Tyc, Boyadjian, & Devanne, 2005). Animal studies evaluating arm and auditory exercises have shown similar altered representations in the motor cortex (Nudo, Milliken, Jenkins, & Merzenich, 1996) and somatosensory cortex (Recanzone, Schreiner, & Merzenich, 1993) following training. These alterations can last for at least several days following termination of exercise practice (Karni & Bertini, 1997; Nudo, et al., 1996),

suggesting that lasting effects of rehabilitation are reflected in plasticity of these regions and mimic that seen in natural recovery.

To clarify the characteristics of training that influence this plasticity, physiotherapy research has investigated the effects of both strengthening (Carroll, Riek, & Carson, 2002; Griffin & Cafarelli, 2007; Hauptmann, Skrotzki, & Hummelsheim, 1997; Rasch & Morehouse, 1957) and skill rehabilitation programmes (de Leon, Hodgson, Roy, & Edgerton, 1998a; de Leon, et al., 1998b; Nudo, et al., 1996; Recanzone, et al., 1993) on corticomotor function and have also contrasted outcomes of the two (Jensen, Marstrand, & Nielsen, 2005; Liu-Ambrose, et al., 2003; Remple, et al., 2001; Risberg, Holm, Myklebust, & Engebretsen, 2007). Because repetitive practice which does not progressively challenge motor execution is thought to be insufficient to prompt plasticity in the motor cortex (Plautz, Milliken, & Nudo, 2000), the increase in strength following isokinetic and isometric exercise is widely believed to result from morphological changes in muscle structure as a result of hypertrophy (enlargement of muscle fibres) (Esposito, et al., 2005; Folland & Williams, 2007; Kanehisa, et al., 2002; Rasch & Morehouse, 1957) and changes of muscle fibre types (Burkhead, et al., 2007). However, assessments in the early stages of strength training programmes show disproportionately larger increases in muscle strength compared to muscle size (Folland & Williams, 2007), suggesting some neural adaptations in the early phases of strength training (Burkhead, et al., 2007). Burkhead et al. (2007) suggest that these adaptations occur in the nervous system and facilitate more efficient motor unit recruitment. Rasch and Morehouse (1957), however, propose that these early strength gains are attributable to practised movement. They explain how repetition of the same movement may assist with postural adaptations, which increase maximal force applied to the target movement as well as refine and improve control over the motor pattern. This idea is supported by the finding that repetitive movements without a strength component have been shown to increase corticomotor excitability, but only for the first 10-25 s following conclusion of exercise (Hauptmann, et al., 1997), reinforcing the idea of a learning component or movement adaptations involved in the early phase of exercise.

Conflicting findings following strength training have been generated from studies assessing cortical excitability using TMS-induced MEPs. Strength training of upper arm (Jensen, et al., 2005) and finger muscles (Carroll, et al., 2002) did not increase, and may even have had an

inhibitory effect (Carroll, et al., 2002), on corticomotor excitability. Conversely, strength training of a lower leg muscle was found to facilitate corticomotor excitability, suggesting a possible difference in the response from upper- and lower-limb muscles to strength training (Griffin & Cafarelli, 2007).

Skill training or training programmes that challenge routine motor execution have been shown to influence corticomotor excitability related to movement (Jensen, et al., 2005; Remple, et al., 2001). There is increasing evidence that limb rehabilitation following stroke is most effective when exercise is incorporated into functional movements (Hogan et al., 2006; Nelles, Jentzen, Jueptner, Muller, & Diener, 2001). These findings are based on both post-treatment functional movement outcomes (described in Section 10.4.1.1 above) and changes in neuroimaging measures such as PET (Nelles, et al., 2001) and TMS-induced MEPs (Ziemann, Muellbacher, Hallett, & Cohen, 2001). Increased amplitude and/or decreased latency of MEPs has been shown following functional rehabilitation programmes in patients with hemiplegia of the arm and/or leg secondary to stroke (Koski, Mernar, & Dobkin, 2004; Piron, Piccione, Tonin, & Dam, 2005) suggesting increased excitability in the corticospinal pathways as a result of such rehabilitation programmes. Greater representation of a movement in the motor cortex (Ziemann, et al., 2001) and reorganised activation of brain structures involved in motor programming and execution (Nelles, et al., 2001) have also been documented after rehabilitation involving functional movement practice.

Specific to muscles involved in swallowing, a series of studies have documented increased size of cortical representation of the tongue (Sessle et al., 2007; Sessle et al., 2005; Svensson, Romaniello, Arendt-Nielsen, & Sessle, 2003; Svensson, Romaniello, Wang, Arendt-Nielsen, & Sessle, 2006) and increased excitability (Svensson, et al., 2003; Svensson, et al., 2006) of the same projections after a tongue protrusion exercise (see Sessle, et al., 2007, for review). Despite these increases in the tongue motor cortex, the authors report that no increase was seen in representation of the “cortical masticatory area/swallow cortex” (Sessle, et al., 2005, pg 111 - 112), suggesting task specificity of plasticity in the motor cortex. The finding that centrally stored motor commands reflect movements that are regularly carried out, i.e., are altered with exercise and return to “normal” once exercise ceases, further reinforces the importance of rehabilitation exercises replicating everyday activity (Keefe, 1995; Nudo, et al., 1996). In relation to neural plasticity associated with recovery of swallowing impairment,

plasticity of the undamaged hemisphere appears to be related to natural recovery of swallowing function following stroke (Barritt & Smithard, 2009; Hamdy, et al., 1998b; Hamdy, et al., 2000).

One study aimed to evaluate the effects of effortful-swallowing on excitability of cortical projections to the swallowing muscles in healthy participants (Gallas, et al., 2009) and found significant increases after 1 week of daily practice lasting 15 minutes. While this study indicates some promise for the effects of effortful-swallowing on corticobulbar function associated with swallowing, baseline values were not reported, and different stimulation methods were used for pre- and post-treatment time-points, making objective evaluation of their findings difficult. Additionally, values obtained from the first author suggest that trials were treated as independent values for analysis, therefore falsely increasing the chances of significant findings.

#### **10.4.2 The role of sensory feedback in the recovery of motor function**

Proprioception is afferent feedback to the brain from muscle mechanoreceptors (Moreau & Moreau, 2001) and is facilitated by visual and vestibular information (Rose & Christina, 2006). This information interacts to provide the sensation of joint movement and position (Lephart, Pincivero, Giraldo, & Fu, 1997). Proprioceptive information during a movement may be disrupted by injury to the mechanoreceptors located in the muscle (Moreau & Moreau, 2001), the neural regions responsible for the processing of this information, or the pathways connecting the two (Gow, et al., 2004b). It is well known that afferent signals carrying proprioceptive information are an essential modulatory element of motor output in variable environments (Edgerton, Tillakaratne, Bigbee, de Leon, & Roy, 2004). Physiotherapy literature advocates that deficiencies of proprioceptive acuity result in delayed reflexive muscle contraction (Wallace, Beard, Gill, & Carr, 1997) and decreased functional motor performance (Borsa, Sauers, & Lephart, 1999; Lephart, Giraldo, Borsa, & Fu, 1996). The interplay between motor output and sensory input is further highlighted by the finding that proprioceptive deficits seen following injury move towards restoration with functional rehabilitation (Lephart, et al., 1997).

Task-oriented training programmes inherently incorporate proprioceptive facilitation (Borsa, et al., 1999). The incorporation of proprioception has been documented to influencing



strength outcomes to a greater extent than strength training (Liu-Ambrose, et al., 2003). This greater increase in strength despite training at submaximal levels of muscle contraction is thought to result from improved movement coordination and neural adaptations as a result of proprioceptive facilitation (Liu-Ambrose, et al., 2003). This assumption fits with the theory proposed by Rasch and Morehouse (1957) that early strength gains are attributable to movement practice. The greater strength improvements documented after skill training that facilitates proprioception are therefore likely to result from the increased opportunity to practise the target movement. Adler and colleagues (2008) suggest that such neuromuscular training is effective for treatment of upper-extremity deficits caused by both poor coordination and muscle weakness.

Task-oriented rehabilitation programmes provide an opportunity for task-specific proprioceptive systems to be stimulated through repetition of meaningful activity. A specificity of learning phenomena has also been shown with afferent stimuli, with a lack of improvements generalizing from trained to untrained sensory skills (Karni & Bertini, 1997; Recanzone, et al., 1993). This suggests that task-specific proprioceptive experiences during training are important for generalization to functional outcomes. Rose and Christina (2006) argue that if proprioceptive information encountered during practice contributes considerably to accuracy of the target movement it will be integrated into the centrally stored motor pattern, regardless of whether it is explicit or implicit in nature. The development of centrally stored motor patterns is highly dependent on the proprioceptive feedback encountered during repetitive practice (Borsa, et al., 1999; Rose & Christina, 2006), as are the neural plasticity mechanisms that aid functional recovery (Edgerton, et al., 2004). For these reasons, facilitation of proprioception is considered critical in functional physiotherapy rehabilitation programmes (Holmich, 1997; Lephart, et al., 1997).

Some studies have investigated the function of proprioception in the swallowing process. Proprioceptive signals from the jaw muscles (through trigeminal afferent fibres) are necessary for coordination of the jaw with muscles of the larynx (Zhang, Yang, Pendlebury, & Luo, 2005), tongue (Zhang, Luo, & Pendlebury, 2001; Zhang, Pendlebury, & Luo, 2003) and visceral processes such as saliva production and respiratory changes (Zhang, et al., 2005). Other swallowing literature has shown afferent information from the face, pharynx and

esophagus contribute significantly to motor output of the swallowing musculature (Hamdy, et al., 1997; Hamdy, et al., 1998a).

### **10.4.3 Considerations for dysphagia rehabilitation techniques**

Many studies have documented superior outcomes for task-oriented skill training over strength training programmes (Liu-Ambrose, et al., 2003; Risberg, et al., 2007). An increase in corticomotor excitability (Jensen, et al., 2005), plasticity of the motor cortex (Remple, et al., 2001), greater functional movement improvements (Risberg, et al., 2007), and greater strength gains (Liu-Ambrose, et al., 2003) collectively suggest task-oriented skill training programmes are more favourable for recovery of motor impairments than strength training programmes.

As suggested by Adler and colleagues (2008), proprioceptive training is effective for treatment of poor coordination and muscle weakness. These two physiologic deficits are common causes of dysphagic symptoms following central nervous system and cranial nerve injury (Huckabee & Pelletier, 1999), signifying the importance of proprioception in dysphagia management. However, the majority of the rehabilitation techniques currently used to treat dysphagia target muscle strengthening only (Burkhead, et al., 2007).

Application of this information to the comparison of head-lift manoeuvre and effortful-swallowing implies that because effortful-swallowing is task-oriented it provides task-specific neuromuscular control training and proprioceptive facilitation relevant to swallowing. Therefore, treatment programmes based on effortful-swallowing may have a greater impact on corticobulbar function and functional motor outcomes than those based on the head-lift manoeuvre. The finding that skill-training techniques assist with strength and coordination of movement suggests that effortful-swallowing may not only be able to strengthen the swallowing musculature but also improve coordination of swallowing. As head-lift manoeuvre is aimed at strengthening peripheral muscles out of the functional context of swallowing, the biomechanical effect it has on muscle strength during swallowing may not translate to adaptive neural changes nor have any observable effect on coordination of swallowing. Furthermore, in the case of patients undergoing rehabilitation to restore pharyngeal swallowing function, training that does not engage the swallowing neural

mechanisms, such as the head-lift manoeuvre, may actually further *decrease* function (Kleim & Jones, 2008) and cortical representations of swallowing (Robbins, et al., 2008).

The reported positive influences of head-lift manoeuvre on swallowing outcomes (Easterling, 2008; Easterling, et al., 2005; Shaker, et al., 2002; Shaker, et al., 1997) implies the exercise protocol (three times per day for six weeks) is sufficient to increase muscle size, as the physiotherapy literature does not support the idea that strength training induces changes in the corticomotor excitability associated with movement. The fact that this increase in strength is transferred to improved swallowing function is also not accounted for in the physiotherapy literature. The increased activation of these muscles during swallowing suggests that functional transfer of strength may be seen in untrained tasks for swallowing at least, or represent cross-over of functions controlled by corticobulbar pathways. This idea is supported by findings that vocal exercise can influence swallowing biomechanics (El Sharkawi et al., 2002), and evidence of neurophysiologic relationships between swallowing, respiratory, articulatory and phonatory systems (Robbins, et al., 2008). Another explanation, as proposed by Robbins (2008), is that by increasing the strength of a component of the swallowing response, the swallowing response may be more efficiently engaged as a result of the amplified component.

## 10.5 Directions for future research

There are very few studies that provide insight into the long-term effects of head-lift manoeuvre and none specific to effortful-swallowing. The efficacies of both head-lift manoeuvre and effortful-swallowing have been demonstrated through biomechanical changes of normal swallowing (Easterling, et al., 2005; Hind, et al., 2001; Huckabee, et al., 2006) and disordered swallowing (Lazarus, et al., 2002; Shaker, et al., 2002), during or following technique execution. A decrease in pulmonary compromise also validates use of these techniques in some disorders of swallowing (Bulow, et al., 2001; Shaker, et al., 2002). Biomechanical evaluations and measures of pulmonary status are relatively short-term assessments of rehabilitation outcomes. Hogan et al. (2006) caution using biomechanical measures as indicators of recovery, and suggest coordination measurements as more representative of restorative function. Although positive biomechanical changes in swallowing suggest both techniques have clinical application for facilitating swallowing function when muscle strength is diminished, the role they play in rehabilitation via changes

in neural pathways and/or activations is unclear (Martin, 2009; Robbins, et al., 2008), i.e., when organisation, initiation, or modulation of muscle activation is impaired. It is necessary to consider the influence of dysphagia rehabilitation techniques not only on motor function but on plasticity of neural processes associated with the swallowing pattern (Burkhead, et al., 2007; Martin, 2009) so effective dysphagia management plans can be developed according to neurophysiologic deficits. Gaining a clear understanding of the underlying neural mechanisms in which plasticity processes work presents an enormous challenge due to the complexity of swallowing.

To clarify the ongoing issues surrounding the efficacy of dysphagia treatment techniques, it is crucial to determine whether task-oriented or non-task-oriented swallowing exercises are most advantageous for facilitating recovery. It remains unknown if the reported changes in swallowing function following treatment manoeuvres are a result of muscle hypertrophy, neurophysiologic changes, or a combination of the two. Unlike limb exercise, guiding accurate practice of the swallowing sequence is not possible. As the effects of practising a maladaptive swallowing sequence have not been documented, verification of the advantages of task-oriented exercise for biomechanical and neurophysiological adaptations is required. Detailing changes in motor function and corticobulbar function associated with both types of exercise is required to provide the much needed evidence for current dysphagia management techniques (Martin, 2009; Robbins, et al., 2008)

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## Chapter 11: Hypotheses for treatment study

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### 11.1 Corticobulbar excitability

#### *Hypothesis 1*

##### **Research question**

No studies have documented the effects of effortful-swallowing on submental MEPs elicited during swallowing. Furthermore, no studies have assessed cumulative effects of treatments on swallowing MEPs.

##### **Hypothesis**

MEPs from the submental muscles during *volitional swallowing* will increase in area following six weeks of effortful-swallowing exercise.

##### **Rationale**

While one study has failed to document immediate changes in volitional swallowing MEPs following neuromuscular electrical stimulation (Doeltgen, et al., 2010a), another study has found differences as a result of olfactory and gustatory input (Wahab, et al., 2010). This suggests that excitability of corticobulbar projections to the submental muscles activated during swallowing can be modulated with some treatment techniques. Increases in MEPs have been documented following task-oriented exercise programmes for limb muscles (Koski, et al., 2004; Piron, et al., 2005). The effect of task-oriented swallowing exercise on corticomotor function needs to be determined.

##### **Significance**

Assessing changes in excitability of cortical projections to the swallowing muscles *during* swallowing will provide insight into the effect of task-oriented training on corticobulbar functions specific to the target movement. While one study has suggested repetitive effortful-swallowing may increase excitability of projections to the submental muscles at rest (Gallas, et al., 2009), it is not known how the technique affects pathways activated during swallowing. As effortful-swallowing is a task-oriented exercise, any influence the technique has on corticobulbar functions would presumably infiltrate those specific to the task, i.e., swallowing. Furthermore, as swallowing MEPs are sensitive to detecting immediate treatment

effects (Wahab, et al., 2010), documenting their responsiveness to cumulative effects will enhance their application as a treatment outcome.

### **Proposed study**

Submental MEPs will be recorded during volitional swallowing in 20 participants, both before and after six weeks of effortful-swallowing. Training will involve three sessions of 33 effortful swallows per day, five days per week (see Section 12.3.6.2 for further details).

## ***Hypothesis 2***

### **Research question**

No studies have documented the change in MEPs recorded during volitional contraction of the submental muscles following effortful-swallowing.

### **Hypothesis**

MEPs recorded during volitional *contraction* of the submental muscles will increase in area following six weeks of effortful-swallowing training.

### **Rationale**

There is inconclusive evidence that MEPs recorded from the submental muscles during rest may be influenced by repetitive effortful-swallowing (Gallas, et al., 2009). Immediate facilitation of submental MEPs recorded during volitional contraction has been documented following sensory swallowing treatments (Doeltgen, et al., 2010a; Wahab, et al., 2010). Additionally, increased amplitude of MEPs occurs as a result of functional rehabilitation programmes in patients with hemiplegia of the arm and/or leg secondary to stroke (Koski, et al., 2004; Piron, et al., 2005).

### **Significance**

One study has documented a change in volitional contraction MEPs but was unable to analyse such change in swallowing MEPs due to no similar change in swallowing MEPs (Doeltgen, et al., 2010a). The authors propose this reflects different levels of cortical involvement for the tasks. Comparison of changes in volitional contraction and volitional swallowing MEPs will provide insight into differential effects of effortful-swallowing on cortical input to the submental muscles for swallowing and non-swallowing tasks.

### **Proposed study**

Submental MEPs will be recorded during volitional contraction in 20 participants, both before and after six weeks of effortful-swallowing. Training will involve three sessions of 33 effortful swallows per day, five days per week.

### ***Hypothesis 3***

#### **Research question**

While there is some evidence that head-lift manoeuvre may facilitate biomechanical aspects of swallowing (Easterling, 2008; Easterling, et al., 2005; Shaker, et al., 2002; Shaker, et al., 1997), the influence the manoeuvre has on corticomotor function is unknown.

#### **Hypothesis**

MEPs from the submental muscles during volitional swallowing will not differ in area from baseline measures following six weeks of modified head-lift exercise.

#### **Rationale**

MEPs recorded from limb muscles both at rest and during contraction are reportedly unaffected by strengthening exercise in the absence of task-oriented practice (Jensen, et al., 2005). Therefore, such training is unlikely to influence pathways specific to swallowing if changes are not documented for non-specific projections to the target muscles.

#### **Significance**

Isolated strength training exercise of limbs reportedly has no effect on functional movement outcomes (Liu-Ambrose, et al., 2003; Rasch & Morehouse, 1957; Remple, et al., 2001; Symons, et al., 2005; Van Peppen, et al., 2004) or corticomotor excitability (Jensen, et al., 2005). This suggests that because the head-lift manoeuvre may positively influence swallowing biomechanics (Easterling, 2008; Easterling, et al., 2005; Shaker, et al., 2002; Shaker, et al., 1997), it may also influence underlying neural mechanisms. Unlike limb exercise, guiding practice of an accurate swallowing sequence in the face of impairment is impossible. While the effects of practising a maladaptive swallowing sequence is unknown, non-task-oriented exercise may be preferred if influences on corticobulbar function associated with swallowing are similar or superior to task-oriented exercise.

### **Proposed study**

MEPs will be recorded from the submental muscles during volitional swallowing in 20 participants, both before and after six weeks of modified head-lift manoeuvre. Training will involve three sessions per day, five days per week. Each session will involve 30 isokinetic head-lifts, and three isometric head-lifts (see Section 12.3.6.1 for further details) held for 30 s (adapted from Shaker, et al., 1997, see Section 10.3.2 for rationale for decreased isometric hold duration).

### ***Hypothesis 4***

#### **Research question**

The influence of the head-lift manoeuvre on excitability of cortical projections to the submental muscles is unknown.

#### **Hypothesis**

MEPs from the submental muscles during volitional contraction will not differ in area from baseline measures following six weeks of modified head-lift exercise.

#### **Rationale**

The head-lift manoeuvre strengthens the submental muscles through repetition of non-task-oriented exercise. Strengthening exercises that do not progressively challenge motor execution with a skill component are not considered to facilitate excitability of cortical projections to the trained muscles (Carroll, et al., 2002; Jensen, et al., 2005) either at rest or during active contraction (Jensen, et al., 2005).

#### **Significance**

The differences in composition and neural command processes documented between swallowing and limb musculature (Chhabra & Sapienza, 2007) together with the possible biomechanical improvements seen following head-lift manoeuvre suggest that some adaptations to corticomotor functions associated with swallowing are possible as a result of the exercise. As MEPs from limb muscles elicited during active muscle contraction are not influenced by non-task-oriented strength training, documenting MEPs during volitional submental muscle contraction allows a comparison between swallowing and limb functions. Additionally, if volitional contraction MEPs are influenced differentially to those obtained



during volitional swallowing, more specific insight into the mechanisms influenced by this exercise can be gained.

### **Proposed study**

MEPs will be recorded from the submental muscles during volitional contraction in 20 participants, both before and after six weeks of modified head-lift manoeuvre. Training will involve three sessions per day, five days per week. Each session will involve 30 isokinetic head-lifts, and three isometric head-lifts held for 30 s (adapted from Shaker, et al., 1997, pp., see Section 10.13.12 for rationale for decreased isometric hold duration).

## **11.2 Pharyngeal pressure**

### ***Hypothesis 5***

#### **Research question**

There are discrepancies in the literature regarding the immediate effects of effortful-swallowing on pharyngeal pressures. Furthermore, while the studies to date provide some insight into the compensatory application of the technique, i.e., how pharyngeal pressures are influenced *during* execution of effortful-swallowing, they do not assess the cumulative effects of repetitive execution on pharyngeal pressures during non-effortful-swallowing.

#### **Hypothesis**

Oropharyngeal and hypopharyngeal pressures during non-effortful volitional swallowing will increase when compared with baseline measures following six weeks of effortful-swallowing training.

#### **Rationale**

Although no studies have investigated the cumulative effect of effortful swallow as an isolated treatment on swallowing biomechanics, oropharyngeal (Lazarus, et al., 2002; Ohmae, et al., 2000; Pouderoux & Kahrilas, 1995) and hypopharyngeal (Huckabee, et al., 2005; Huckabee & Steele, 2006) pressures have been shown to increase during execution of effortful-swallowing. While some studies have not replicated these findings (Bulow, et al., 1999, 2001), the statistical power of these studies may have been insufficient to detect the changes documented by others. Additionally, improved swallowing function has been reported for patients exhibiting – among other symptoms – reduced pharyngeal contraction

(Crary, 1995; Huckabee & Cannito, 1999) following rehabilitation including effortful-swallowing.

### **Significance**

Further research is required to clarify the effects of effortful-swallowing on pharyngeal pressures so the technique can be more precisely prescribed according to physiologic deficits. Documenting any cumulative effects on pharyngeal pressures resulting from effortful-swallowing as an isolated rehabilitation technique is crucial to justify its prescription with the aim of facilitating bolus flow through increased pharyngeal pressure. By investigating cumulative effects, the translation of documented immediate effects to swallowing biomechanics during non-effortful volitional swallowing can be confirmed or refuted.

### **Proposed study**

Oropharyngeal and hypopharyngeal pressure will be recorded during volitional swallowing in 20 participants, both before and after several weeks of effortful-swallowing. Training will involve three sessions of 33 effortful swallows per day, five days per week.

## ***Hypothesis 6***

### **Research question**

A facilitation of UES relaxation has been documented during execution of effortful-swallowing. Low correlations between submental sEMG measures and UES pressures suggest that the decreased UES pressures are unlikely to be a result of increased submental muscle activation alone. The mechanisms behind these adaptations in UES pressures need to be elucidated. Additionally, while findings suggest that effortful swallow may assist with UES opening during execution of the task, the cumulative effects of the technique on UES pressures during non-effortful-swallowing has not been documented.

### **Hypothesis**

The magnitude of nadir pressures in the UES during volitional swallowing will increase when compared with baseline measures following six weeks of effortful-swallowing exercise.

### **Rationale**

There is no evidence regarding the cumulative effects of effortful-swallowing as an isolated rehabilitation technique on UES pressures during non-effortful-swallowing. However, during execution of the technique, increased magnitude of nadir pressure has been documented (Huckabee, et al., 2005; Witte, et al., 2008). Additionally, patients demonstrating impaired bolus flow through the UES as one component of severe swallowing impairment have shown improved function following rehabilitation involving effortful-swallowing (Crary, 1995; Huckabee & Cannito, 1999).

### **Significance**

By documenting various cumulative effects of the technique alongside changes in UES pressures, the cause of the increased magnitude of nadir pressures previously documented can be further elucidated. Increased magnitude of UES nadir pressures represent less resistance for bolus transfer into the esophagus, and increased hyolaryngeal traction force on the UES (Jacob, et al., 1989). If effortful-swallowing has the same cumulative effect on UES pressures as those documented during execution of the technique, long-term change in swallowing physiology can be assured through prescription of this technique.

### **Proposed study**

Nadir UES pressures will be recorded during volitional swallowing in 20 participants, both before and after several weeks of effortful-swallowing. Training will involve three sessions of 33 effortful swallows per day, five days per week.

## ***Hypothesis 7***

### **Research question**

Discrepancies in the literature exist regarding the cumulative effects of head-lift manoeuvre on swallowing biomechanics, suggesting further research is required. The influence of the technique on pharyngeal contact pressures during swallowing is unknown. The effects of head-lift manoeuvre on pharyngeal pressures is limited to one study (Shaker, et al., 1997), which documented decreased hypopharyngeal intrabolus pressure following the exercise. As intrabolus pressure fluctuates considerably relative to frictional forces, velocity and viscosity (Brasseur & Dodds, 1991; Olsson, et al., 1994), the cause of this decrease may be unrelated to treatment effects.

## **Hypothesis**

Oropharyngeal and hypopharyngeal pressures during volitional swallowing will not differ from baseline measures following six weeks of modified head-lift manoeuvre exercise.

## **Rationale**

As the head-lift manoeuvre is not designed to enhance pharyngeal or oral muscle contraction, closure of the larynx, lips or velopharyngeal port or tongue movement (factors responsible for pharyngeal pressure generation, Perlman & Christensen, 1997), it is unlikely the exercise will influence pharyngeal pressures.

## **Significance**

The head-lift manoeuvre was devised to facilitate UES opening by increasing the strength of the submental muscles. Documenting the cumulative effect of the head-lift manoeuvre on pharyngeal pressures will provide insight into the biomechanical adaptations that result from the technique.

## **Proposed study**

Oropharyngeal and hypopharyngeal pressure will be recorded during volitional swallowing in 20 participants, both before and after six weeks of modified head-lift manoeuvre. Training will involve three sessions per day, five days per week. Each session will involve 30 isokinetic head-lifts, and three isometric head-lifts held for 30 s (adapted from Shaker, et al., 1997, see Section 10.3.2 for rationale for decreased isometric hold duration).

## ***Hypothesis 8***

### **Research question**

While studies suggest maximum opening of the UES may be facilitated following six weeks of the head-lift manoeuvre, the results don't appear to be specific to the technique. Furthermore, how spatial measures of UES opening documented with VFS translate to functional UES swallowing pressures is unclear.

## **Hypothesis**

Magnitude of nadir pressures in the UES during volitional swallowing will increase when compared with baseline measures following six weeks of modified head-lift manoeuvre exercise.

## **Rationale**

The head-lift manoeuvre aims to create greater traction force of hyolaryngeal excursion to assist with opening of the UES (Ferdjallah, et al., 2000; Hamdy, Xue, Valdez, & Diamant, 2001; Shaker, et al., 2002). A greater degree of UES opening has been reported as a result of six weeks of head-lift exercise (Easterling, et al., 2005; Shaker, et al., 2002; Shaker, et al., 1997), as well as a decrease in hypopharyngeal intrabolus pressure (Shaker, et al., 1997), known to signify less resistance for the descending bolus (Brasseur & Dodds, 1991). Greater anterior displacement of the *larynx* has been documented to result from the head-lift manoeuvre (Easterling, et al., 2005; Shaker, et al., 2002; Shaker, et al., 1997), which contributes to UES opening during swallowing (Miller, 1999). These findings together suggest that the magnitude of UES nadir pressures is likely to increase as a result of biomechanical adaptations, namely increased traction force on the UES from hyolaryngeal excursion (Jacob, et al., 1989).

## **Significance**

UES measures from participants who have completed the head-lift manoeuvre protocol need to be contrasted with another exercise technique to clarify whether UES adaptations are specific to the head-lift manoeuvre. Establishing how previously reported changes in UES biomechanics measured using VFS translate to swallowing pressures will assist in determining whether head-lift manoeuvre affects the function of the UES during swallowing. As the technique was designed to fulfil this purpose, it is proposed that facilitation of UES pressures will be an outcome of the technique. However, these presumed effects need to be documented to ensure accuracy in treatment planning for patients with UES dysfunction.

## **Proposed study**

Nadir UES pressures will be recorded during volitional swallowing in 20 participants, both prior to and following six weeks of modified head-lift manoeuvre exercise. Training will involve three sessions per day, five days per week. Each session will involve 30 isokinetic

head-lifts, and three isometric head-lifts held for 30 s (adapted from Shaker, et al., 1997, see Section 10.3.2 for rationale for decreased isometric hold duration).

## **11.3 Muscle hypertrophy**

### ***Hypotheses 9***

#### **Research question**

The response of the submental muscles to strengthening exercise, such as the effortful swallow and the head-lift manoeuvre is unknown.

#### **Hypothesis**

Cross-sectional area of the anterior belly of digastric and geniohyoid will increase when compared with baseline measures following six weeks of effortful-swallowing exercise.

#### **Rationale**

Implementation of effortful-swallowing results in greater activation of the submental musculature (Huckabee, et al., 2005). While no studies have looked at the cumulative effect of effortful-swallowing on CSA of the submental muscles, greater activation documented during the technique implies that repetitive execution may induce changes in submental muscle morphometry.

#### **Significance**

Enlargement of muscles resulting from strength training signifies adaptations in the size and number of muscle fibres (Folland & Williams, 2007). If such changes are documented in the submental muscles following neuromuscular exercise, reversal of atrophy of these muscles secondary to disease and/or aging can be proposed through such treatments.

#### **Proposed study**

CSA of the anterior belly of the digastric and the geniohyoid muscles will be calculated from ultrasound images prior to and following six weeks of effortful-swallowing exercise. Training will involve three sessions of 33 effortful swallows per day, five days per week.

## ***Hypotheses 10***

### **Research question**

As for Hypothesis 9, the response of the submental muscles to strengthening exercise, such as the effortful swallow and the head-lift manoeuvre is unknown.

### **Hypothesis**

Cross-sectional area of the anterior belly of digastric and geniohyoid muscles will increase when compared with baseline measures following six weeks of modified head-lift manoeuvre exercise.

### **Rationale**

Head-lift manoeuvre activates the submental muscles in both an isometric and isokinetic fashion to increase muscle strength (Ferdjallah, et al., 2000; Hamdy, et al., 2001; Shaker, et al., 2002). An eight-week isometric lingual exercise programme for the tongue (270 repetitions per week) reportedly increased lingual volume, as shown by MRI (Robbins, et al., 2005; Robbins, et al., 2007).

### **Significance**

See Significance for Hypothesis 9.

### **Proposed study**

CSA of the anterior belly of the digastric and the geniohyoid muscles will be calculated from ultrasound images prior to and following six weeks of modified head-lift manoeuvre exercise. Training will involve three sessions per day, five days per week. Each session will involve 30 isokinetic head-lifts, and three isometric head-lifts of 30 s duration (adapted from Shaker, et al., 1997, see Section 10.3.2 for rationale for decreased isometric hold duration).

## **11.4 Hyoid displacement**

### ***Hypothesis 11***

#### **Research question**

Unchanged (Wheeler-Hegland, et al., 2008) or decreased (Bulow, et al., 1999; Hind, et al., 2001) hyoid and laryngeal displacement has been documented during effortful-swallowing when compared with non-effortful-swallowing. However, no study has assessed whether

these results are reinforced in non-effortful swallows following extended periods of effortful-swallowing exercise.

### **Hypothesis**

Anterior hyoid displacement during non-effortful volitional swallowing will not differ from baseline measures following six weeks of effortful-swallowing exercise.

### **Rationale**

While one study has documented increased *duration* of displacement during effortful-swallowing, the extent of displacement was not as great as was found for non-effortful-swallowing (Hind, et al., 2001). Reduced maximal hyoid displacement was also documented by Bulow and colleagues (1999). Another study has documented no change in hyoid displacement during the technique (Wheeler-Hegland, et al., 2008)..

### **Significance**

As effortful-swallowing is frequently prescribed as a rehabilitation technique, cumulative effects must be documented to provide insight beyond compensatory applications. The cumulative effects of the technique on anterior hyoid displacement during non-effortful swallows needs to be determined to decipher if such effects mimic those reported during execution of effortful-swallowing. This is especially pertinent in light of the reported negative influence on anterior hyoid excursion documented by some studies during effortful-swallowing. By documenting cumulative changes in hyoid displacement, aligning the treatment to specific physiologic impairments will be more precise. Additionally, it will ensure that exacerbation of reduced hyoid displacement in certain patients is avoided.

### **Proposed study**

Measures of anterior hyoid displacement will be calculated from dynamic ultrasound video recordings prior to and following six weeks of effortful-swallowing exercise. Training will involve three sessions of 33 effortful swallows per day, five days per week.



## ***Hypothesis 12***

### **Research question**

There are inconclusive findings regarding the effect of the head-lift manoeuvre on hyolaryngeal excursion. Furthermore, the similar activation levels documented in the muscles above and below the hyoid implies that negative effects on hyolaryngeal excursion could potentially result. More research is required to confirm how the head-lift manoeuvre influences hyoid displacement during swallowing.

### **Hypothesis**

Anterior hyoid displacement during volitional swallowing will not differ from baseline measures following six weeks of modified head-lift manoeuvre exercise.

### **Rationale**

Head-lift manoeuvre has been shown to result in greater anterior displacement of the *larynx*. However, this effect is not generalized to other components of hyolaryngeal excursion, specifically superior or anterior displacement of the hyoid or superior displacement of the larynx. This may be due in part to the activation of infrahyoid muscles during the exercise that possibly counteract the effect of greater anterior pull on the hyoid from the strengthened submental muscles.

### **Significance**

The head-lift manoeuvre is designed to strengthen the submental muscles for greater traction force on the hyoid and larynx (Ferdjallah, et al., 2000). The anterior component of hyolaryngeal excursion is crucial for UES opening, and also for airway protection. While these components of the swallow may be assisted by anterior movement of the larynx, they also rely on anterior displacement of the hyoid bone. Elucidating the effect of the head-lift manoeuvre on anterior hyoid displacement will provide more evidence for the suitable physiologic deficits to be addressed by the technique.

### **Proposed study**

Measures of anterior hyoid displacement will be calculated from dynamic ultrasound video recordings prior to and following six weeks of modified head-lift manoeuvre exercise. Training will involve three sessions per day, five days per week. Each session will involve 30

isokinetic head-lifts, and three isometric head-lifts of 30 s duration (adapted from Shaker, et al., 1997, see Section 10.3.2 for rationale for decreased isometric hold duration).

## **11.5 Muscle activation**

### ***Hypothesis 13***

#### **Research question**

While effortful-swallowing is known to increase submental muscle activation at the time of execution, the cumulative effects of the technique on the output of these muscles is not known. To assess the rehabilitative potential of the technique, its cumulative effect on non-effortful-swallowing needs to be determined. Additionally, as swallowing is executed with submaximal muscle strength (Robbins, Levine, Wood, Roecker, & Luschei, 1995), it is unclear if increases resulting from effortful-swallowing will transfer to increases during non-effortful-swallowing.

#### **Hypothesis**

Amplitude of submental muscle activation during volitional swallowing will increase compared with baseline measures following six weeks of effortful swallow.

#### **Rationale**

Greater submental muscle activation has been documented during execution of effortful compared with non-effortful swallows (Huckabee, et al., 2005; Wheeler-Hegland, et al., 2008). Additionally, task-oriented training programmes for limb muscles have been shown to positively influenced strength outcomes related to the target movement (Liu-Ambrose, et al., 2003; Risberg, et al., 2007).

#### **Significance**

Documenting the cumulative effects of effortful-swallowing on submental muscle activation during non-effortful volitional swallowing will elucidate whether the technique has a rehabilitative effect on swallowing physiology. As most swallowing rehabilitation techniques aim to increase muscle strength (Burkhead, et al., 2007), despite swallowing requiring submaximal levels of muscle activation, changes in muscle activation during swallowing will provide insight into the importance of muscle strength in non-effortful-swallowing.

### **Proposed study**

Amplitude of submental muscle activation during volitional swallowing will be calculated from sEMG recordings prior to and following six weeks of effortful-swallowing exercise. Training will involve three sessions of 33 effortful swallows per day, five days per week.

### ***Hypothesis 14***

#### **Research question**

While increased sEMG measures have been documented during effortful-swallowing, the cumulative effects of the technique on maximal muscle output are unknown.

#### **Hypothesis**

Amplitude of submental muscle activation during maximal voluntary contraction will increase compared with baseline measures following six weeks of effortful-swallowing exercise.

#### **Rationale**

Effortful swallow has been shown to increase submental muscle activation at the time of execution (Huckabee, et al., 2005; Wheeler-Hegland, et al., 2008). While no studies have investigated the cumulative effect of the exercise on non-effortful dry swallows, repetitive effortful-swallowing – and therefore increased submental muscles activation – is likely to increase strength of these muscles.

#### **Significance**

By comparing muscle activation during swallowing with that recorded during maximal output, the importance of overall muscle strength for swallowing can be assessed. If increased muscle activation is documented for volitional contraction following six weeks of effortful-swallowing exercise, the exercise can be presumed to challenge and enhance maximal submental muscle strength.

### **Proposed study**

Amplitude of submental muscle activation during maximal voluntary contraction will be calculated from sEMG recordings prior to and following six weeks of effortful-swallowing exercise. Training will involve three sessions of 33 effortful swallows per day, five days per week.

## ***Hypothesis 15***

### **Research question**

While it has been proposed that increased anteroposterior UES opening documented after six weeks of head-lift manoeuvre is due to an increase in submental muscle activation during swallowing (Shaker, et al., 2002), this has not been explicitly demonstrated. Implications of submental muscle strengthening following the head-lift manoeuvre have been made from fatigue analysis studies. Strengthening is presumed based on the finding that these muscles demonstrate fatigue during the isometric head-lift (Ferdjallah, et al., 2000; Jurell, et al., 1997). Only one study has documented muscle fatigue before and after the head-lift exercise protocol for comparison of activation levels (White, et al., 2008). This study suggests that while strength gains are likely in the sternocleidomastoid muscle, the same changes are not seen in the submental muscles (White, et al., 2008). How the measure used in this study (fatigue resistance) translates to muscle activation changes following the exercise is unclear.

### **Hypothesis**

Amplitude of submental muscle activation during volitional swallowing will not differ from baseline measures following execution of six weeks of modified head-lift manoeuvre.

### **Rationale**

While the head-lift manoeuvre aims to strengthen the submental muscles through isokinetic and isometric muscle contractions (Shaker, et al., 1997), a specificity of practice phenomenon (Rose & Christina, 2006) is observed for strength training exercises, with a lack of transfer of strength improvements observed for untrained tasks (Liu-Ambrose, et al., 2003; Rasch & Morehouse, 1957).

### **Significance**

Knowledge of how fatigue resistance in the submental muscles translates to muscle strength during swallowing is crucial to document if activation of these muscles is enhanced as a result of the exercise. As the head-lift manoeuvre was devised facilitate UES opening by strengthening the submental muscles, documenting changes in sEMG and UES opening is crucial to provide empirical evidence for the technique. Additionally, by comparing the outcomes of head-lift exercise with results from the effortful-swallowing, comparisons can be

made between task-oriented and non-task-oriented exercise regarding the optimal method for enhancing muscle activation for swallowing.

### **Proposed study**

Amplitude of submental muscle activation during volitional swallowing will be calculated from sEMG recordings prior to and following six weeks of modified head-lift manoeuvre exercise. Training will involve three sessions per day, five days per week. Each session will involve 30 isokinetic head-lifts, and three isometric head-lifts of 30 s duration (adapted from Shaker, et al., 1997, see Section 10.3.2 for rationale for decreased isometric hold duration).

## ***Hypothesis 16***

### **Research question**

It is unclear how the head-lift manoeuvre affects maximal output of the submental muscles (see Research question, Hypothesis 15). While less fatigue resistance has been documented in the submental muscles following the exercise protocol, it is unclear how this translates to maximal muscle strength.

### **Hypothesis**

Amplitude of submental muscle activation during maximal voluntary contraction will increase compared with baseline measures following six weeks of modified head-lift manoeuvre exercise.

### **Rationale**

Isometric and isokinetic strengthening exercise of limb muscles result in increased strength of the target muscles (Esposito, et al., 2005; Folland & Williams, 2007; Sekir, et al., 2007). Head-lift manoeuvre recruits the submental muscles in both an isometric and isokinetic manner.

### **Significance**

Documenting changes in maximal output of the submental muscles will provide insight into the effects the technique on overall muscle strength. Comparing changes in maximal voluntary contraction sEMG and swallowing sEMG will provide insight into the mechanisms of muscle activation influenced by a non-task-oriented strengthening exercise.

### **Proposed study**

Amplitude of submental muscle activation during maximal voluntary contraction will be calculated from sEMG recordings prior to and following six weeks of modified head-lift manoeuvre exercise. Training will involve three sessions per day, five days per week. Each session will involve 30 isokinetic head-lifts, and three isometric head-lifts of 30 s duration (adapted from Shaker, et al., 1997, see Section 10.3.2 for rationale for decreased isometric hold duration).

## **11.6 Additional research questions**

### ***Corticobulbar excitability***

As all available research investigating the effects of swallowing treatments on corticobulbar excitability have examined immediate effects of techniques, i.e., in the first 1-2 hours following completion of the treatment, this study will also record blocks of 15 MEPs during volitional contraction and volitional swallowing at the following time points after the first exercise session: < 5 min, 30 min, 60 min, and 90 min. These results will allow comparison of effects between the current study and previous investigations. Additionally, investigation of onset latencies will also be completed on the data obtained for immediate and cumulative treatment effects.

### ***Pharyngeal pressure***

Some studies have reported a sensitivity of pharyngeal pressures measured with manometry to various bolus types (Butler, et al., 2009). This raises the possibility that bolus swallows may respond differently than dry swallows to the treatments. For this reason, 10 mL water bolus swallows will be collected during baseline and post-treatment assessments, and compared for determining the effect of either treatment on these swallows.

Additionally, as the cumulative effects of repetitive effortful-swallowing are not understood, there is a possibility that the technique may not influence non-effortful swallows. To determine if effortful-swallows and/or non-effortful swallows are influenced by repetitive execution of the technique, effortful swallows will also be assessed at pre-exercise and post-exercise time points. As both the exercises being examined in this study involve strengthening components, assessing their effects on a strengthening manoeuvre (such as effortful-swallowing) will help to elucidate what, if any, mechanisms are influenced by such exercise.

## Chapter 12: Methodology

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### 12.1 Participants

40 healthy research participants over the age of 50 years (52 – 83 years, mean age 69 years) were recruited for participation in this study. Interested research participants were provided with an information sheet for review and given verbal information regarding the nature and scope of the project. Participants were contacted approximately a week later to ascertain if they wished to proceed as a participant. At this time, an appointment was made at the Swallowing Rehabilitation Research Laboratory at the Van der Veer Institute for commencing the study. This study received ethical approval from the Upper South B Regional Ethics Committee, New Zealand.

#### 12.1.1 Consent and exclusion criteria

Participants reported no history of neurological or muscular disorder/disease affecting pharyngeal anatomy, specifically no history of stroke or dysphagia. Participants were excluded if they had previous head and/or neck surgery or injury. If participants reported a history of gastroesophageal reflux disease (GERD), the researcher ascertained the severity and whether they had undergone any surgical interventions for GERD. Participants were included if symptoms were reported to be mild and managed with proton pump inhibitor medication (PPI). The inclusion of these participants was based on evidence that shows no significant differences between GERD patients and healthy controls for average UES resting pressures, or nadir deglutitive relaxation pressures (Kwiatek, Mirza, Kahrilas, & Pandolfino, 2009). Six participants (three males and three females, and three from each exercise group) reported they had previously experienced mild GERD symptoms with two of these currently taking PPI medications (one from each exercise group). No participant was taking medications that would likely interfere with their swallowing abilities.

Participants underwent single pulse TMS. Although there are no known risk factors of single pulse transcranial magnetic stimulation (Chokroverty et al., 1995), caution is advised when stimulating participants with a long-standing history of poorly controlled seizures, or a family history of epilepsy (Chokroverty, et al., 1995) therefore, participants were excluded if either

of these criteria applied. Further precautions were taken and excluded participants from completing MEP procedures if they had metal fragments in the head outside the mouth (such as shrapnel or surgical clips), implanted devices (such as cardiac pacemakers or medical pumps), frequent or severe headaches, or those who were pregnant. Participants completed a questionnaire to ensure they meet inclusion criteria (Appendix II).

## 12.2 Instrumentation

### 12.2.1 MEP instrumentation

The system used for MEP data acquisition was custom designed and the various system components are described below.

#### *12.2.1.1 SEMG measurement for determining MEP threshold*

Skin cleansing swabs (70% v/v isopropyl alcohol mediswab, 36001000, BSN Medical, VIC, Australia) were used to prepare skin for recording electrodes. Recording electrodes (neonatal solid gel electrodes, BRS-50K, blue sensor) were connected via a shielded cable (Shielded Bio Amp cable, MLA2540, ADI Instruments) to an EMG amplifier (Dual Bio Amp, ML 135, ADI Instruments) which was connected to the recording system (Powerlab 8/30, ML 870, ADI Instruments) (Figure 12.1). Muscle activity was monitored using the Scope software which is commercially available for use with the Powerlab system. Data were acquired at a rate of 10 kHz. High-pass filtering of 10 Hz and low pass filtering of 2 kHz was employed. The system channel that triggered a recording sweep was coupled to the output trigger of the transcranial magnetic stimulator. This connection prompted the Scope software to record a sweep of 260 ms duration, with every discharge of the magnetic stimulator. Each sweep recorded data 100 ms pre-trigger and 160 ms post-trigger. Sweeps were triggered on the uprisings slope of the measured sEMG signal.



*Figure 12.1. Shielded cable connected to the Bioamp system.*



### 12.2.1.2 Trigger device

A custom-built trigger device<sup>27</sup> (Figure 12.2) monitored the continuous sEMG signals which were sent from the amplifier (Bioamp) to the recording system (Powerlab). The trigger device produced a single transistor-transistor logic (TTL) pulse when the monitored sEMG signal reached a pre-set threshold. This threshold was set to 75% of the individual's mean sEMG peak amplitude for 10 swallows for recording motor-evoked potentials, and was consistent across measurement sessions within an individual. Subsequent to production of the TTL pulse, the trigger device was disabled for 10 s to allow the individual to rest and to avoid unintentional production of a trigger stimulus. This rest period was signalled by an orange indicator light which switched off to indicate the system was again receptive to sEMG triggering. The trigger device was coupled (via output channel) with the magnetic stimulator (via input channel).



Figure 12.2. Custom-built trigger system.

### 12.2.1.3 Magnetic stimulator

Cortical transcranial stimulation was conducted using a commercially-available magnetic stimulator (Magstim 2002, Magstim Company Limited, Whitland, Wales) (Figure 12.3). A figure-of-8 coil with an outer wing diameter of 70 mm (Figure 12.4) and a maximum output of 2.2 Tesla was used (2nd Generation Double 70mm Coil, 3190-00, Magstim Company Ltd, Whitland, Wales).

<sup>27</sup> Swallowing Stimulator, R. Dove, Department of Medical Physics and Bioengineering, Canterbury District Health Board, Christchurch, New Zealand, 2007



*Figure 12.3. Magnetic stimulator used for transcranial stimulation of the cortical projections to the submental muscles.*



*Figure 12.4. Figure 8 coil used for focal transcranial magnetic stimulation of the cortical projections to the submental muscles.*

#### ***12.2.1.4 Analysis software***

A custom-designed software package (described in Chapter 7) was used to quantify onset latency (see Method F, Section 7.2.3, page 111) and MEP area (see Method K, Section 7.2.3, page 113). Data initially recorded as Scope files were saved as text files and opened in the UC Evoked Potential Analysis software version 3.15. The software displays each MEP as an individual waveform, with options for rectification and averaging (Figure 12.5).

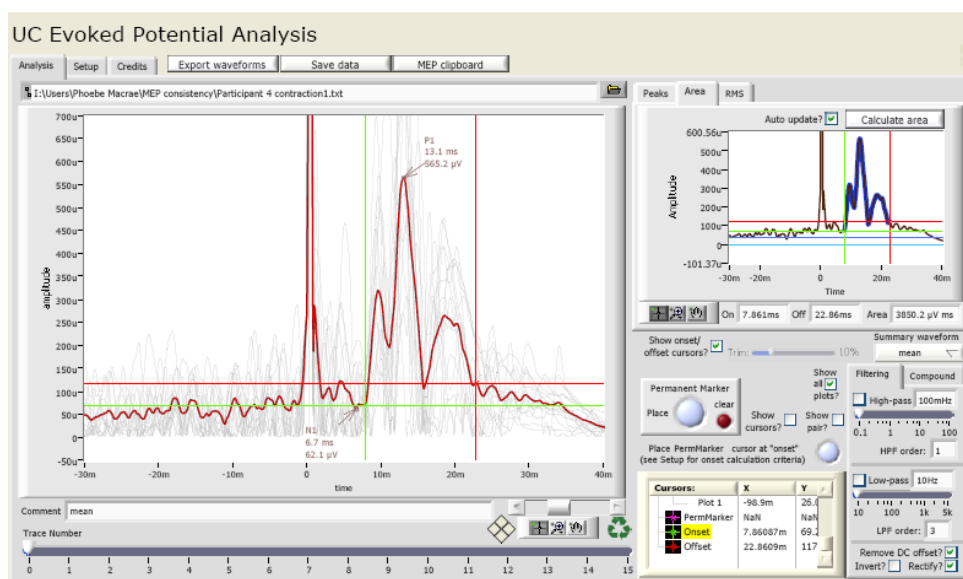


Figure 12.5. Rectified and averaged waveform displayed in the UC Evoked Potential Analysis software. See Chapter 7 for details regarding onset latency and area calculation.

### 12.2.2 Manometry instrumentation

A 100-cm-long round catheter, 2.1 mm in diameter (Model CTS3 + EMG, Gaeltec, Hackensack, NJ), was used for manometric data collection. The catheter houses three solid-state, unidirectional, posteriorly-oriented sensors (2 x 5 mm) spaced 30 mm between the midpoints of sensors 1 and 2 and 20 mm between the midpoints of sensors 2 and 3 (Figure 12.6). Pressures were measured in the upper pharynx, mid pharynx and upper esophageal sphincter (UES) with sensors 1, 2, and 3 respectively. Data were acquired using the Kay Elemetrics Digital Swallowing Workstation. Digitized 12-bit samples were obtained with a sampling frequency of 500 Hz and displayed in a -100 to 500-mmHg display window. The catheter was calibrated at 500 mmHg at room temperature. The system software generates pressure waveforms as a function of time. All measurements were displayed on a computer monitor during data collection and digitally recorded for offline analysis.



Figure 12.6. Pharyngeal manometry catheter with three solid-state sensors.

### 12.2.3 Ultrasonography instrumentation

A Phillips™ IU22 model ultrasonography device was used with a 12-5 MHz linear array transducer (Figure 12.7) for coronal grey-scale images used to obtain submental muscle cross-sectional area (CSA). 2D gain, depth, and focus settings were adjusted for individual anatomy. Settings established as optimal for each participant were documented and used for subsequent scans.



*Figure 12.7. Philips 12-5 MHz linear array transducer used for coronal CSA measures of the submental muscles.*

A 5-1 MHz curved array transducer (Figure 12.8) was used for sagittal real time grey-scale video loop acquisition of a swallow event. Video loops were 8 s duration, recorded at 49 or 51 frames/s, depending on the depth, focus points, and 2D gain applied to the individual's image. The resolution/speed setting was set to the highest frame rate per second. 2D gain, depth, and focus settings were adjusted for individual anatomy. Settings established as optimal for each participant were documented and used for subsequent scans.



*Figure 12.8. Philips 5-1 MHz curved array transducer used for sagittal measures of hyoid displacement.*

### 12.2.4 sEMG instrumentation

The recording system for sEMG measures is the same as described for the sEMG recording for MEP threshold (see Section 12.2.1.1). Once the sweep was triggered, data from 500 ms

pre-trigger and 2100 ms post-trigger was recorded. Sweeps were triggered on the uprising slope of the measured sEMG signal.

### 12.2.5 Biofeedback instrumentation

Skin cleansing swabs (70% v/v isopropyl alcohol mediswab, 36001000, BSN Medical, VIC, Australia) were used to prepare the skin over the submental muscles. A triode electrode pad (T3402M Triode™, Thought Technology Ltd, Canada) was placed on the skin. These electrodes were connected to the MyoTrac portable biofeedback system (MyoTrac EMG system, T9900, Thought Technology Ltd, Canada) for sEMG biofeedback sessions for the effortful-swallowing exercise group (Figure 12.9). The software program displays a continuous waveform representative of real-time EMG recording. Waveforms are displayed with time on the horizontal axis, and amplitude on the vertical axis. A horizontal cursor can be set to an adjustable threshold to provide a visual target for sEMG activity.



*Figure 12.9. MyoTrac portable biofeedback system used for sEMG biofeedback during home visits for participants in the effortful-swallowing group.*

## 12.3 Procedure

Each participant was seen for an initial assessment session, during which numerous baseline measures were made. Following the baseline session, participants carried out six weeks of exercise, either modified head-lift manoeuvre or effortful swallow. Participants were then seen for an outcome session at which time measures made during the baseline session were repeated to assess the effect of exercise on these measures.

Measures taken during the baseline and outcome sessions were designed to assess swallowing function at numerous levels of control. Cortical excitability of projections to the submental muscles was assessed as a measure of corticomotor function and neural conduction. Pharyngeal pressures and hyoid displacement were measured, using manometry and ultrasound respectively, to assess swallowing biomechanics. Cross-sectional area and activation magnitude of the submental muscles were measured with ultrasound and sEMG respectively, to assess morphometry and activation of the end-point of the swallowing system, specifically the submental muscles.

### **12.3.1 Baseline session**

During the baseline session the following measures were assessed:

- Latency and magnitude of neural transmission from primary motor cortex (M1) to submental muscles, assessed using motor evoked potentials (MEPs) induced by single pulse transcranial magnetic stimulation (TMS).
- Pharyngeal pressure generation in the oropharynx and hypopharynx, and in the upper esophageal sphincter (UES) during regular saliva swallows, effortful swallows, and 10 mL water bolus swallows, measured with a pharyngeal manometric catheter.
- Extent of hyoid displacement during swallowing, measured using real-time gray-scale sagittal ultrasonography video loops.
- Cross-sectional area (CSA) of submental muscles (anterior belly of digastric and geniohyoid muscles), assessed using grey-scale coronal ultrasonography images.
- Level of submental muscle activation during volitional swallowing and volitional contraction, measured using sEMG.

### **12.3.2 Procedure for MEPs**

#### ***12.3.2.1 MEP preparatory procedures***

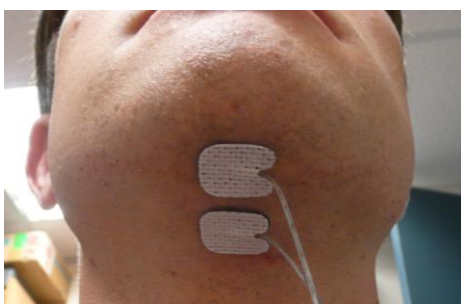
Participants were seated in a comfortable chair and the skin over the zygomatic arch and under the chin were cleaned with an alcohol swab before three surface electrodes were adhered. Two of the electrodes were placed at midline over the submental muscle group, under the chin. The participant was asked to sit comfortably with a neutral head position, and asked to avoid neck flexion while the electrodes were being placed. This ensured that the electrodes were not touching and were adhered to the skin surface once the participant was

comfortably positioned. The anterior electrode was placed so that its lateral edge was in line with the medial, inferior bony edge of the mandible. It overlapped each side of the midline by 1 cm. The posterior recording electrode was placed so there was an approximately 5 mm gap between the lateral edges of the two recording electrodes. This electrode also overlapped the midline 1 cm on each side. Electrodes were placed so the connecting wires were on the same side (Figure 12.10). These electrodes served as sEMG recording electrodes. A ground electrode was adhered to the skin over the bony prominence of the zygomatic arch (Figure 12.11).

After being connected to the Powerlab data acquisition system, two baseline measures were recorded. The two measures were counterbalanced across participants and within a participant across sessions.

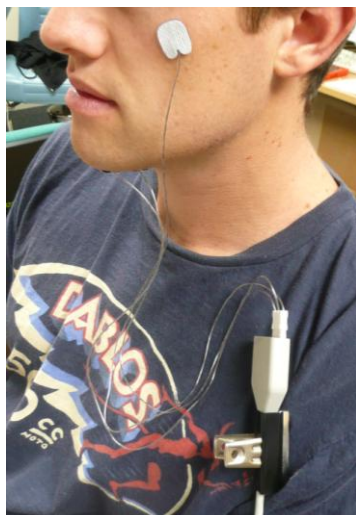
### **sEMG baseline measures during volitional swallowing**

The threshold for triggering the magnetic stimulator during acquisition of MEPs was identified by having research participants perform 10 non-effortful saliva swallows. Peak sEMG amplitudes were recorded and the mean peak sEMG amplitude calculated. Seventy-five percent of this mean was defined as the threshold for the trigger device to send a TTL impulse to the TMS, and therefore initiate a recording sweep. Electrode placement was at midline on the submental muscle group, making sEMG recordings vulnerable to extrinsic and intrinsic tongue muscle activation. For this reason, participants were asked to minimize tongue movement during swallows. They were also asked to avoid movement of the jaw or tongue during the period that swallows were being recorded to prevent the trigger threshold from being breached during non-swallowing activity. All MEPs recorded for an individual during the baseline and outcome sessions were triggered at the same degree of muscle contraction so within-participant measures were comparable.



*Figure 12.10. Placement of recording electrodes used to measure MEPs from submental muscles.*





*Figure 12.11. Placement of the ground electrode over the zygomatic arch for recording MEPs.*

### **sEMG baseline measures during volitional contraction of the submental muscles**

Participants were provided instructions for volitionally contracting their submental muscles. This was explained as follows: “Imagine you need to yawn and you are trying to do so discreetly”. If participants were unable to master the task (as evidenced by sEMG biofeedback), a further instruction was provided as follows: “Use the muscles in your cheeks to prevent the yawn from opening your jaw”. Once this task has been mastered, the participant completed 10 repetitions of maximal submental muscle contraction. These measures were used for sEMG pre- and post-exercise comparisons.

sEMG biofeedback was used to encourage participants to roughly ‘match’ the sEMG signal of their volitional contractions with that of their volitional swallows. This was done in preparation for MEP data collection to reduce any variation in MEP size that may have been introduced as a result of different levels of perceived muscle effort between the volitional swallowing and volitional contraction conditions. Trigger thresholds were also set at the same level of sEMG activity for both volitional swallowing and volitional contraction for this reason.

### **Identifying the optimal scalp location for eliciting submental MEPs**

The optimal site for acquiring MEPs was identified prior to baseline MEP measurements. For this, the cranial vertex ( $C_z$ ) was identified and marked on the scalp according to the



International 10-20 electrode system (Klem, Luders, Jasper, & Elger, 1999). Participants were instructed to volitionally contract their submental muscles (see above). During this time the trigger threshold was set to supra-sEMG levels so that manual triggering could be carried out by the researcher. Starting at the left hemisphere, the researcher discharged the TMS over numerous points covering the area approximately 4 cm anterior, and 8-10 cm lateral to  $C_z$  (representing the primary motor cortex). One transcranial magnetic stimuli was discharged with each contraction, over a single point on the primary motor cortex. The same procedure was repeated over the right hemisphere. The hemisphere producing the largest MEP was defined as “swallowing dominant” and was used for subsequent MEP data collection. The point on that hemisphere at which the largest MEPs were recorded was defined as the optimal site for acquiring submental muscle MEPs. This site was marked on the scalp using a water soluble pen and was used for subsequent MEP data collection. Measurement of the optimal site’s location with reference to its lateral and anterior position from  $C_z$  was recorded for subsequent MEP data collection. Photos were also taken of the location in relation to the hairline as a secondary check for re-locating the optimal site for eliciting submental MEPs in the outcome session (Figure 12.12).

### **Stimulus response curve**

Following location of the optimal site for MEP recording, the stimulus intensity of the TMS was set to 30%. The researcher adjusted the trigger threshold to 75% of the participant’s sEMG mean for volitional swallows, and positioned the coil over the optimal site for eliciting MEPs. The participant was instructed to volitionally contract the submental muscles. Stimulus intensity was kept at 30% while three MEPs were recorded. Stimulus intensity was then increased in 5% increments, with three MEPs recorded at every increment until MEP amplitudes plateaued or max stimulator output was reached. This provided quantification of the largest possible MEP elicited from the hotspot.



*Figure 12.12. Markings made of the coil position at the hotspot relative to the hairline.*

## **Setting stimulus intensity level**

TMS intensity was set to the level that evoked MEP amplitudes of approximately 50% of the maximum MEP response elicited during the stimulus response curve. Five trials were conducted at the lower stimulus intensity to assure that MEPs were approximately half the size of maximal MEPs. This size was chosen to allow adequate range for growth or reduction in MEP size in response to exercise. The stimulus intensity was kept consistent for all MEP data collection for the same participant.

### ***12.3.2.2 MEP baseline measures***

Baseline measures of submental MEPs were collected for volitional swallowing and volitional contraction conditions. For each condition, 15 MEPs were triggered at the hot spot of the swallowing dominant hemisphere at the prior identified TMS intensity.

## **12.3.3 Procedures for manometry**

Prior to inserting the manometric catheter, participants were instructed on task completion. A triode electrode pad was placed on the skin overlying the submental muscle group. These electrodes were connected to the MyoTrac portable biofeedback system and were used for training the participant for master of the effortful swallow technique. The researcher requested the participant swallow their saliva as they normally would. Participants visualized the sEMG waveform on the computer screen and following an instruction to “swallow hard with all the muscles in your mouth and throat” (Hind, et al., 2001), attempted to double the amplitude of EMG activity recorded with regular saliva swallows (Wheeler-Hegland, et al., 2008). Once mastery of this task was evident, the participant was disconnected from the biofeedback device and seated in upright in a dental chair for catheter placement. Catheter calibration was conducted according to the manufacturer’s specifications, prior to data collection for each participant.

### ***12.3.3.1 Catheter placement***

The lubricated intraluminal catheter was inserted in the naris chosen by the participant. Once the tip of the catheter reached the upper pharynx, identified by resistance at the posterior pharyngeal wall, the participant was asked to tilt their head towards the ceiling to reduce the oropharyngeal angle. Once the catheter reached the upper pharynx, the participant returned

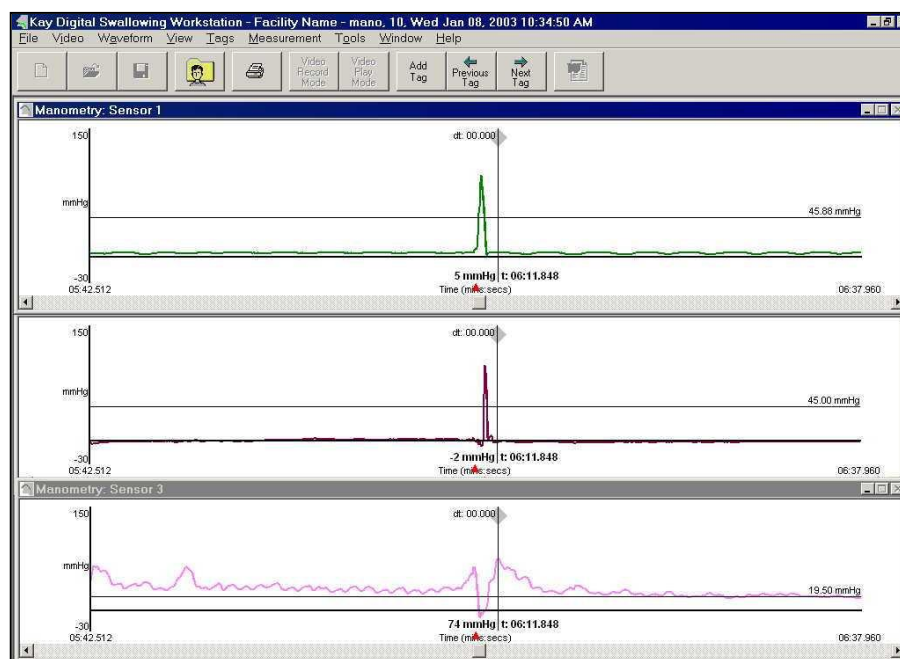
their head to a neutral position they ingested water rapidly through a straw until the catheter was pulled down approximately 35 cm into the proximal esophagus (Figure 12.13).



*Figure 12.13. Transnasal insertion and stabilization of the manometric catheter.*

The catheter was then slowly pulled back out until correct catheter placement was confirmed through visualization of the typical ‘M’ wave displayed during swallowing at sensor 3 (Figure 12.14), indicating placement in the proximal aspect of the UES (Gumbley, et al., 2008; Huckabee, et al., 2005; Huckabee & Steele, 2006; Witte, et al., 2008).

Sensors were oriented towards the posterior pharyngeal wall (Huckabee, et al., 2005; Huckabee & Steele, 2006). Sensor 1 was therefore located in the oropharynx approximately even with the base of the tongue, sensor 2 in the hypopharynx approximately even with the laryngeal additus, and sensor 3 in the tonically contracted UES. Once the correct placement of the catheter was identified, the catheter was taped securely to the outside of the nose with medical tape (3M Micropore™ hypoallergenic surgical tape, 1533-0) to avoid displacement during swallowing. Participants were given a few minutes to adjust to the sensation of the catheter before commencing swallowing tasks and were seated so they were unable to view the waveforms displayed on the computer monitor. The distance from the third sensor to the nose tip for session 1 was noted by recording the number imprinted on the catheter at the entrance of the nose. For subsequent manometric data collection, the catheter was inserted into the same naris, and to the same distance in mm from the tip of the nose as was determined optimal in the baseline session.



*Figure 12.14. Manometry waveforms displayed on the Kay Elemetrics Digital Swallowing Workstation. The top (green) waveform represents data acquired from the uppermost sensor, approximately even with the base of tongue, the middle (red) waveform represents data acquired from the second sensor, at approximately the level of the laryngeal additus, and the lower (pink) waveform represents data acquired from the lowermost sensor, or the UES. The higher baseline values recorded in the 3<sup>rd</sup> sensor represent the tonic contraction of the UES. The 'M' shape seen in the 3<sup>rd</sup> waveform implies placement in the proximal aspect of the UES.*

### **12.3.3.2 Manometry baseline measures**

Following the adjustment period, participants performed five repetitions of three swallowing tasks: regular saliva swallows, effortful swallows, and 10 mL water bolus swallows. Participants were prompted to swallow whenever they felt comfortable, following a 30 s rest period. Dry swallows were performed first to alleviate any effect of the effortful swallow on subsequent dry swallows. The order of the effortful swallow and the 10 mL water bolus swallow was then counter-balanced according to exercise group and gender. In total, participants performed 15 swallows. As two of the three conditions evaluated in this study did not involve ingestion of a bolus and as simultaneous fluoroscopy was not performed, pressure measurements reflected contact pressure rather than intrabolus pressure. Contact pressure reflects the pressure created by pharyngeal tissue coming together, and thus represents pharyngeal clearance pressure (Witte, et al., 2008).

### 12.3.4 Procedures for ultrasonography

To control for potential variation in neck flexion, a dental bite-block was developed for each participant and secured to one arm of a transducer stabilization stand (Figure 12.15).



*Figure 12.15. Bite-block attached to upper arm of transducer stabilization stand.*

#### 12.3.4.1 Creation of the dental bite-block

The researcher inspected the participants' mandibular dentition, and selected an appropriate-sized precast acrylic bite-block (Plaque photo, light-curing hybride composite resin, W and P Dental, Germany). After sterilizing their hands, the researcher mixed a two-component Vinyl Polysiloxane Impression Material Putty (3M ESPE Express™ STD) for approximately 60 s. The combined material was then placed on both the superior and inferior surfaces of the bite-block ensuring the material met at the lateral edges. The participant was asked to open their mouths and hold it open until instructed otherwise. The bite-block covered with malleable impression material was positioned in the participants' mouth so that the bite-block was aligned with the teeth. The participant was then asked to bite down slowly and softly on their back teeth until the teeth met the superior and inferior surfaces. Biting was done slowly so that any gaps in the dental structure were filled with impression material. The participant was asked to close their lips around the material and hold their teeth in this position for approximately 2 min. Once the impression material had set, the bite-block was taken out of the mouth and rinsed in cold water. The researcher then put on latex gloves (powder-free microtextured latex gloves, Healthcare Distributors Ltd, Christchurch) and used a scalpel to trim off residual material on the bite-block for greater comfort during swallowing.

#### 12.3.4.2 Positioning of the participant

Participants were seated in a comfortable chair in the ultrasound suite of a private radiology practice. The chair was shifted onto pre-set markers on the 1 m<sup>2</sup> base-plate of the transducer

stabilization stand (Figure 12.16), used to ensure the consistent positioning across sessions. Participants were instructed to sit comfortably with their bottom back in the chair and their head in a neutral position. Once the participant had achieved this posture, they were asked to maintain it while the bite-block was connected to the upper adjustable arm of the stand and brought to a position where they could comfortably place it in the oral cavity in alignment with their teeth (Figure 12.17). Participants needed to adjust posture slightly to accommodate the bite-block but every attempt was made to avoid any flexion of the neck from the rest position by adjusting the arm of the stand in the horizontal and/or vertical plane.



*Figure 12.16. Chair markers to ensure consistent positioning of the chair relative to the transducer stabilization stand.*

#### **12.3.4.3 Ultrasound baseline measures**

Two baseline measures were taken using ultrasonography. Measures were counterbalanced across participants and within participants across sessions.

#### **Cross-sectional area (CSA) measures of floor of mouth muscles**

Images of the geniohyoid and anterior belly of digastric muscles were taken with the participant sitting upright. A generous amount of ultrasound transmission gel (Aquasonic 100) was placed over the transducer surface which was then fixed to the lower arm of the stand. The lower arm of the stand was moved in the horizontal and vertical plane so that the

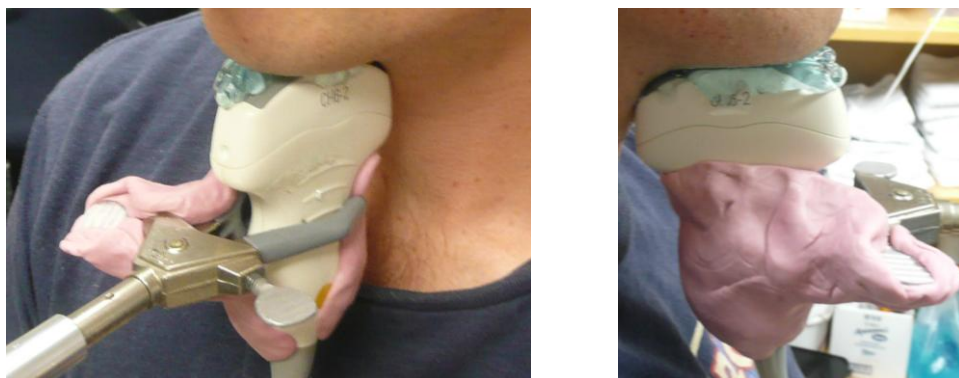


transducer was positioned in a coronal plane, approximately midway between the mentalis of the mandible and the superior palpable edge of the thyroid cartilage. The transducer surface was placed perpendicular to the submental muscle group, with minimal pressure to ensure that transducer pressure did not distort muscle structure (Scholten, et al., 2003). Depth settings were tailored to accommodate individual anatomy, and gain settings were adjusted to allow optimal visualization of muscle borders.



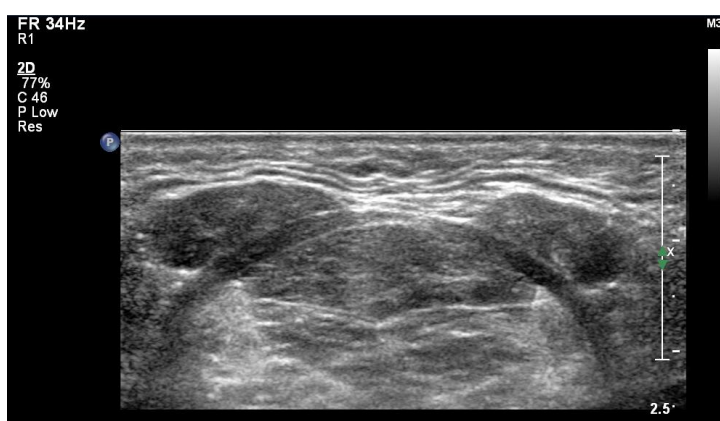
*Figure 12.17. Positioning of the bite-block in the participant's mouth.*

When the target muscles were clearly identified on the screen, a condensation-cured silicone mould (Protesil® labor mixed with Protesil® catalyst gel, Vannini Dental Industry, Italy) was placed around the transducer and arm of the stand to ensure stable and consistent positioning during image acquisition (Figure 12.18). The participant was asked to remain as still as possible while the researcher took still images of the muscles in a relaxed state.



*Figure 12.18. Silicone mould used to encase the transducer for stability during image acquisition and to control transducer placement in future ultrasound assessment.*

Two images were taken and processed offline, with 2D gain settings being adjusted for each image (Figure 12.19). The vertical and horizontal locations of both the transducer stabilization arm and the bite-block arm of the stand were noted on a separate protocol sheet. 2D gain, depth, and focus settings used during each image acquisition were also noted on the protocol sheet. These measurements and the silicone transducer casing were used for subsequent submental CSA measures to ensure stable participant and transducer positioning in the two sessions. The participant then released the bite-block and was given a rest period of 5-10 min before completing the next ultrasound measure (Scholten, et al., 2003).



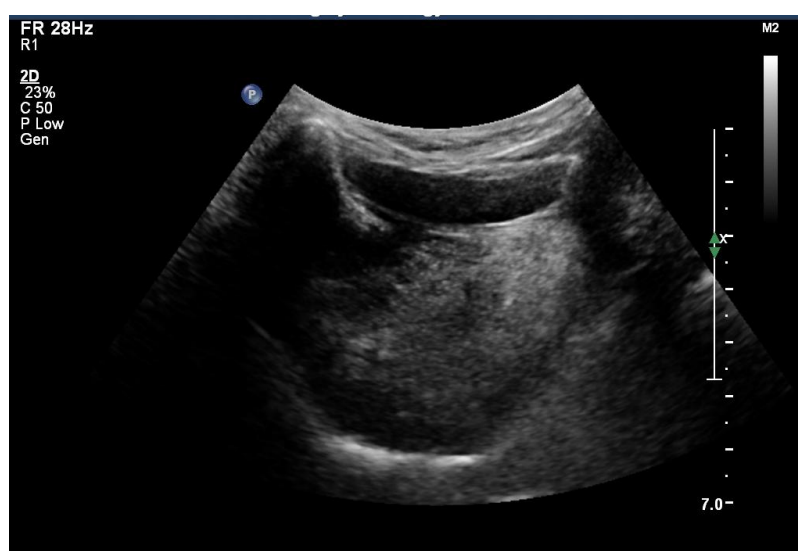
*Figure 12.19. Coronal grey-scale image of the submental muscles. Settings are displayed on the top right corner of the screen. Depth settings are displayed on the bottom right corner of the screen. Note the image appears inverted with the top of the image representing the transducer surface contact with the skin under the chin.*

## **Quantification of hyoid displacement**

The bite-block was positioned in the same place as determined optimal in the floor of mouth measures (see above). The participant then placed the bite-block in the mouth. A generous amount of ultrasound transmission gel (Aquasonic 100) was placed on the C5-1 transducer. The transducer was connected to the lower arm of the stand and placed in a sagittal plane, at approximately midline between the lateral edges of the mandible, perpendicular to the submental muscles. The shadows of the mental spine of the mandible and the hyoid were identified in the image. Depth and focus settings were tailored to accommodate individual anatomy, and gain settings were adjusted to allow optimal visualization of the hyoid and mental spine of the mandible shadow intersections (Figure 12.20). When the images were



clearly visible, the same condensation-cured silicone was used to form a casing around the transducer and arm of the stand to ensure stable positioning during image acquisition. Once the researcher initiated the video loop recording, the participant was prompted to swallow their saliva as they usually would. A time lapse of no less than 30 s occurred between swallows so participants could accrue saliva, therefore minimizing the amount of pre-swallow tongue movement. Again, the vertical and horizontal locations of both arms of the stand were noted on a separate protocol sheet, along with 2D gain, focus, and depth settings. These measurements and the silicone transducer casing were used for subsequent hyoid displacement data collection to ensure stable participant and transducer positioning in both baseline and outcome sessions.



*Figure 12.20. Sagittal view used to measure hyoid displacement. Placement was maintained once clear acoustic shadows of the hyoid and mentalis of the mandible were visualized.*

### 12.3.5 Procedures for sEMG

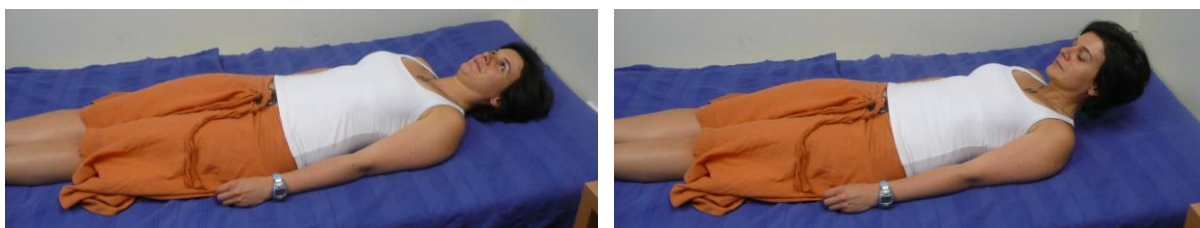
The sEMG baseline measures of swallowing were obtained in preparation for the MEP procedure. sEMG baseline measures of maximal contraction of the submental muscle group were collected at the same time, and are described above (see Section 12.3.2.1). sEMG for both volitional swallows and volitional contractions were counterbalanced. These measures were used to compare sEMG measures obtained at baseline with those obtained following the exercise programme.

### 12.3.6 Exercise programme

Following completion of the baseline session, the first session of the exercise programme was completed at the Swallowing Rehabilitation Research Laboratory at the Van der Veer Institute. The instructions for each participant varied depending on the exercise group they were assigned to. Procedures for the two groups were as follows.

#### 12.3.6.1 *Modified head-lift exercise protocol*

Participants assigned to the modified head-lift manoeuvre exercise group carried out an exercise protocol modified slightly to that outlined by Shaker and colleagues (1997). They lay supine on a padded stretcher bed with their arms by their sides. For the isokinetic component, they were instructed to briefly lift their heads to look at their toes and then rest their heads back on the bed. They repeated the isokinetic head-lift 30 times. For the isometric component, they were then instructed to lift their head to the point where they could see their toes and hold it for 30 s (Figure 12.21). The isometric component was adapted to that reported by Shaker and colleagues (1997), who instructed the hold to last for 1 min. As described in Section 10.3.2, reducing the length of time the isometric component is sustained may inhibit participant drop out by making the goals of the exercise more attainable, while still achieving therapeutic muscle fatigue. The sustained head-lift was repeated a total of three times. Verbal feedback was provided throughout regarding the mastery of task performance.



*Figure 12.21. Modified head-lift manoeuvre exercise protocol.*

#### 12.3.6.2 *Effortful swallow protocol*

As the effortful swallow involves adaptation of pharyngeal swallowing, task mastery is less easily assessed by behavioural observation. Therefore, sEMG of the submental muscle group was employed in the initial exercise session to train participants to the task. Participants assigned to the effortful swallow group had submental electrodes connected to the MyoTrac portable sEMG biofeedback device in order to provide visual biofeedback of muscle activity

to the participant. The participant was instructed to complete a regular saliva swallow. The researcher noted the amplitude of the sEMG signal and adjusted the display screen and horizontal threshold bar. They were then asked to attempt an effortful swallow (as instructed previously during the manometric assessment of pharyngeal pressures), encouraging the participant to make the biofeedback signal touch the horizontal threshold bar (set at approximately double the amplitude of saliva swallows). The researcher noted the amplitude of the effortful swallow and provided auditory feedback as appropriate. For example, if the sEMG signal was the same as the regular swallow, the researcher prompted the participant to swallow harder until the EMG signal approached or breached the horizontal target marker. Effortful swallow was carried out 33 times, in order to match the number of repetitions outlined in the head-lift manoeuvre protocol by Shaker and colleagues (1997). The participant was instructed to aim for the horizontal threshold bar using the sEMG signal during the swallow, which was adjusted according to individual strength.

### **12.3.7 Post exercise MEPs – baseline session**

Following completion of the first exercise session, 15 volitional contraction MEPs and 15 volitional swallowing MEPs were recorded at intervals of 5, 30, 60, and 90 min (see Section 12.3.2.2) to assess the immediate effects of the exercise on excitability of cortical projections to the submental muscles. Studies utilizing MEPs from swallowing musculature have typically used similar time points to document treatment effects (Doeltgen, et al., 2010a; Fraser, et al., 2002; Fraser, et al., 2003; Gow, et al., 2004b; Jefferson, et al., 2009a; Jefferson, et al., 2009b; Mistry, et al., 2006; Mistry, et al., 2007; Power, et al., 2004). This assessment of immediate changes was in addition to cumulative changes recorded following six weeks of exercise practice. Each recording block took approximately 10 min, leaving 20 min between recordings for providing instructions for the home programme and addressing any queries regarding the exercises.

### **12.3.8 Home visits and exercise record sheets**

Each participant was given an exercise record sheet to take home (Appendix III and IV), and instructed to carry out the practised exercise three times per day, five days per week for six weeks. The record sheet had an explanation of the exercise specific to the group the participant had been assigned to, and contact details of the researcher. Each of the three daily sessions involved 33 repetitions of the assigned exercise (30 rapid head-lifts and three

sustained head-lifts for the modified head-lift manoeuvre group, and 33 effortful swallows for the effortful swallow group).

Participants were visited by the primary researcher at home once per week for the duration of their exercise programme. This home visit involved the same procedures as the first exercise session carried out at the swallowing rehabilitation research laboratory. Participants in the effortful swallow exercise group were connected to the portable MyoTrac sEMG biofeedback device. Biofeedback was available only for the weekly visit to monitor mastery of the task and not for daily exercise practice. Participants in the modified head-lift group carried out one exercise session in the presence of the researcher to check procedures.

### **12.3.9 Outcome session**

If possible, the day following completion of six weeks of the exercise programme, each participant was scheduled for a session to obtain post-treatment measurements. If the day immediately following the completion was not possible (weekend, holiday), the first available time was used, with no outcome sessions being longer than 2 days from exercise completion. This session followed the exact procedure outlined for the baseline session to obtain the following measures: submental muscle MEPs for volitional contraction and volitional swallowing; pharyngeal pressures for non-effortful, effortful, and 10 mL water bolus swallows; CSA of submental muscles; hyoid displacement and submental muscle activation during swallowing and maximal contraction. For each measurement, instrumental and participant settings that were used in the baseline session were used again to ensure measures for each participant were comparable across sessions.

## **12.4 Data and statistical analysis**

Statistical analyses were performed in the analysis environment R (R Development Core Team, 2010). R is open-source software created and maintained by statisticians.

Descriptive plots were formulated in Microsoft Excel 2007. All values depicted in the plots were obtained from the raw data. Raw data is presented initially to provide a visual representation of the structure and range of the data used for statistical analysis. The plots illustrate the means for a given measure for each group at each time point. Error bars represent  $\pm 1$  standard deviation of the mean.

Linear mixed-effects models were used to estimate the effects of each treatment on the measures (Gelman & Hill, 2007; Pinheiro & Bates, 2000). The function *lme* from the R package *nlme* was used to fit the models (Pinheiro & Bates, 2000). To model the measure of interest (area, onset latency, amplitude, duration, percent change, or CSA) there was a fixed effect of session, with the intercept and effect of session allowed to vary between participants. Statistical analysis was performed on the raw data. The calculation generated by the model is a t-statistic. While the results of both exercise groups are presented together, each model evaluated each treatment separately, comparing post-exercise measures with baseline measures. As no previous studies have examined the possible effect of these two treatments on the measures utilized in this study, the ultimate aim was to estimate the size of effects resulting from each treatment, an approach recommended for such exploratory work (Robey & Schultz, 1998; Robey, 2004). While this precludes conclusions regarding which of the two treatments is optimal for any given effect, a direct comparison between the two would have been considered if an effect was documented for either treatment, therefore allowing insight into the presence of a difference.

Within- and across-participant standard deviations were obtained from the model, as well as estimated effects and their 95% confidence intervals. Tables report the output of the statistical model. While statistical analysis was completed on the raw data, the output of the model (standard deviations, estimated effects, and confidence intervals) are reported as a percentage of the estimated means from the model in the text (standard deviations) and tables (effects and confidence intervals) for ease in interpreting the relative size of each. Baseline data are not presented in the tables as the structure of the baseline data is provided by the raw data plots preceding all tables. To assess the fit of the models, residual plots were visually inspected for variance unexplained by the model.

The choice of statistical analysis method used for the treatment study differs somewhat to that typically reported in the swallowing literature. Treatment studies often use GLM repeated-measures. A linear mixed-effects model was selected for this analysis because of the advantages it offers over RM-ANOVA (see SPSS Inc., 2002; Gueorguieva & Krystal, 2004 for review). Field (2009) lists three main benefits of multilevel linear models over general linear models, such as the GLM RM-ANOVA. Firstly, linear mixed-effects models do not assume homogeneity of regression slopes. In the model used for this study, the intercept and

effect of session were allowed to vary between participants, which cannot be achieved with GLM RM-ANOVA. This means that differences between the participants at baseline, and differences between the participants in their response to treatment can be accurately accounted for, rather than assuming these are the same across participants. Secondly, Field (2009) identifies the advantage of linear multilevel models in that they do not assume independence between different cases of data. Lastly, and most importantly for the data in the current study, is the benefits in how mixed-effects models handle missing data. Mixed-effects models use all available data, and are not affected by randomly missing data (Gueorguieva & Krystal, 2004). Additionally, the particular model used for this analysis provides absolute values for estimates of effects and the 95% confidence intervals around these, within-participant standard deviations, and group standard deviations. This makes application of these values more contextual when compared with standardized effect sizes. As this study is exploratory, and makes multiple comparisons, achieving statistical significance after corrections for multiple comparisons will be difficult. Therefore, providing estimated effects and their 95% confidence intervals is crucial for gaining some insight into the likely size of effects (Colegrave & Ruxton, 2003). Because this analysis is novel in this field of research, the traditional approach was also completed, using general linear model repeated-measures ANOVA. Details of each RM-ANOVA and the results are presented in Appendix V.

The number of comparisons made from the current data set is 112, giving a Bonferroni adjusted  $p$ -value of 0.0004 for significance at the 0.05 alpha level (Bland & Altman, 1995). The lack of independence of many comparisons in this study makes the Bonferroni method of correction an overly conservative estimate (Bland & Altman, 1995). Because of the extremely low  $p$ -value required to achieve statistical significance, the data are also explored by interpreting confidence interval surrounding the estimated effects. This approach is recommended to provide insight into the presence and size of effects, especially in the case of exploratory research in which numerous comparisons are often made (Colegrave & Ruxton, 2003; Robey & Schultz, 1998; Robey, 2004).

### 12.4.1 MEP data

The 15 MEP traces from both the volitional swallowing and submental muscle contraction tasks recorded within each data block were imported as text files into the UC Evoked Potential Analysis software (described in Chapter 7). For quantitative analysis of MEP onset

latency, the onset of the MEP was subjectively determined from the rectified-average waveform (see Method F, Section 7.2.3, page 111). For quantitative analysis of MEP area, the researcher defined the onset latency, as described above. The offset cursor was then automatically placed at 15 ms following the onset cursor. The area of this 15 ms EMG response was calculated automatically by the software. A 15 ms section of the rectified and averaged waveform was selected prior to the stimulus, the area of which was subtracted from the post-stimulus EMG response (see Method K, Section 7.2.3, page 113). The averaged waveform of the 15 rectified trials was used for calculating both the area and onset latency of each block of MEPs. While this method demonstrated the lowest reliability coefficient for onset latency detection in Chapter 7, the accuracy of this method in estimating area and onset latency was not investigated. As previous literature has recommended this method to ensure phase cancellation does not affect MEP values (see Chapter 7 for discussion), this approach was employed for data analysis in the current study. More research is required to investigate how accuracy of MEP measures is affected by the other methods reported in Chapter 7 before such methods are applied to MEP data analysis. Within-subject area and onset latency values were obtained for both volitional contraction and volitional swallowing at each assessment block (pre-exercise, 5 min, 30 min, 60 min, 90 min, and 6 weeks post-exercise).

### **12.4.2 Manometry data**

The following measures were obtained offline: Peak or nadir pressure for each sensor, defined as the highest (sensors 1 and 2) or lowest (sensor 3) recorded pressure during the swallow; duration of pressure generation for each sensor, defined as the time (s) from onset to offset of pressure generation for sensors 1 and 2 and the time between the highest pressure reading before the UES pressure drop to the highest reading following the drop for sensor 3; peak to peak duration, defined as the time (s) from the highest point in sensor 1 to the highest point in sensor 2; and total duration of swallowing pressure generation, defined as the time between the first observed onset of pressure generation at any sensor and the last offset of pressure at any sensor.

Amplitudes were obtained by highlighting the swallow of interest and selecting the ‘calculate waveform statistics’ option of the Kay swallowing workstation. Durations were obtained by highlighting from the point of pressure onset to the point of pressure offset, and reading the automatically generated time label.

### 12.4.3 Ultrasonography data

#### 12.4.3.1 Hyoid displacement

Prior consensus for placement of the calipers was at the initiation of the spine of the mandible shadow, on the edge closest to the geniohyoid muscle (reference caliper), and the more superior intersection of the hyoid shadow with the geniohyoid muscle (hyoid displacement caliper) (Figure 12.22). From the video loop, the researcher identified a ‘rest’ frame prior to the swallow of interest and a ‘maximal displacement’ frame, at which the hyoid bone was at maximal anterior displacement during each swallow (Figure 12.22). Electronic calipers were used to measure the distance between the mental spine of the mandible and the intersection of the hyoid shadow and the geniohyoid muscle. These images could be saved as images separate from the video loop. Distances were calculated for both the rest and maximal displacement frames. Quantification of hyoid displacement, or the change from resting hyoid distance to maximal displacement distance, was calculated as a percentage of the distance travelled from rest, with resting distance taken as 100%. This was calculated by subtracting the maximal displacement value from the rest value, then dividing the remainder by the rest value and multiplying by 100.

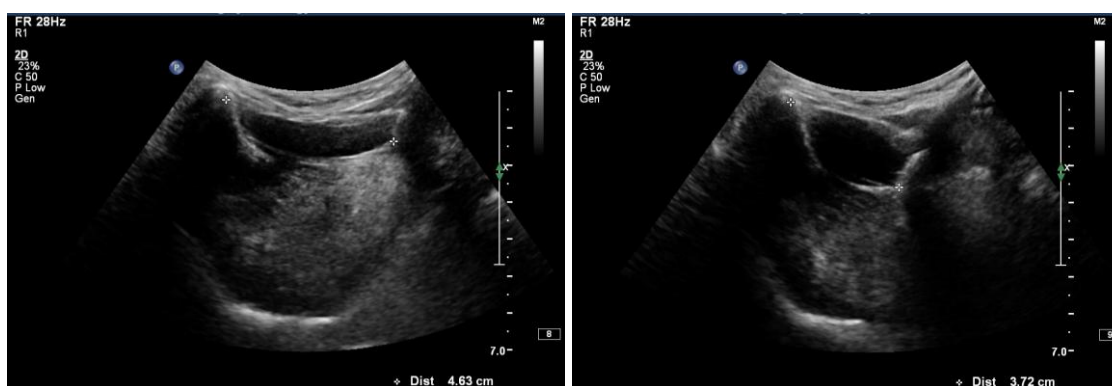


Figure 12.22. Example of the caliper placements used to calculate percent change of hyoid displacement for the ‘rest’ frame (left) and ‘maximal displacement’ frame (right).

#### 12.4.3.2 Cross-sectional area of the submental muscles.

The gray-scale coronal images of the submental muscles were used to determine cross-sectional area (CSA) of the submental muscles. The mylohyoid muscle was unable to be analysed due to an inability to visualize it in many participants, and an inability to determine the outer edges of it in other participants, making it impossible to calculate the CSA. The two



separate bellies of the anterior belly of the digastric muscle, and the paired bellies of the geniohyoid were measured offline using a continuous trace caliper. The continuous trace was used to manually outline the muscle border. A CSA value was obtained for the left belly of the anterior belly of digastric, another for the right belly of the same muscle, and another for the left and right belly of the geniohyoid together due to the difficulty in detecting the midline border between the two bellies in this muscle (Figure 12.23). The continuous trace caliper automatically generated the CSA once the caliper met up with the starting point of the trace. The image containing the CSA measures could be saved as a separate image.



*Figure 12.23. Examples of the continuous trace calipers used to calculate CSA of the two anterior bellies of the digastric muscle, and the geniohyoid muscles collectively. CSA is displayed at the bottom right of the screen.*

#### 12.4.4 sEMG data

For sEMG measures, the 10 maximal submental contraction sEMG traces and the 10 saliva swallow sEMG traces recorded as scope files were saved as text files and analysed with the UC Evoked Potential Analysis software (described in Chapter 7). The 10 repetitions obtained at each data block were averaged to obtain within-subject mean amplitudes.

### 12.5 Inter- and intra-rater agreement

Statistical analysis for inter- and intra-rater agreement was performed using Predictive Analytics SoftWare (PASW, SPSS Release 18.0). An additional investigator analysed 20% of the data from all measures, and the lead investigator analysed 20% a second time. Inter- and intra-rater agreement was analysed using single-measure intra-class correlation coefficients

(ICCs). Excellent agreement was achieved for most measures. The highest inter-rater agreement was observed for amplitude of pharyngeal manometric waveforms. These are computer generated with no subjective assessment required. The lowest inter-rater agreement was observed for judging onset latency of MEP waveforms. This is a subjective measure using relatively noisy data. The highest intra-rater agreement was observed for amplitude of pharyngeal manometric and sEMG waveforms. The lowest intra-rater agreement was observed for assessing percent change of hyoid displacement. ICCs for each measure are shown in Table 12.1.

**Table 12.1. ICCs for inter- and intra-rater agreement.**

<b>Measure</b>		<b>Inter-rater ICC</b>	<b>Intra-rater ICC</b>
<b>Pharyngeal manometric waveforms</b>	Amplitude	1.00	1.00
	Durations	0.89	0.99
<b>Cross sectional area of the submental muscles</b>	left anterior belly of the digastric	0.91	0.97
	right anterior belly of the digastric	0.81	0.98
	Geniohyoid	0.80	0.96
<b>hyoid displacement</b>	Percent change	0.86	0.93
<b>MEP waveforms</b>	Area	0.96	0.99
	Onset latency	0.65	0.98
<b>sEMG waveforms</b>	Amplitude	0.93	1.00

## Chapter 13: Results

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### 13.1 Participants

The mean age of the effortful-swallowing group was 67.5 years (range = 52 – 79). The mean age of the 10 males in the effortful-swallowing group was 68.0 years (range = 57 – 78) and for the 10 females the mean age was 67.0 (range = 52 – 79). The mean age of the modified head-lift group was 70.5 years (range = 53 – 83). The mean age for the 10 males in the modified head-lift group was 73.1 years (range = 60 – 83) and for the 10 females the mean age was 68 years (range = 53 – 77).

### 13.2 Exercise maintenance

Each exercise group had a possible total of 15 exercise units per week to complete (three times per day, five days per week). From analysis of the exercise log sheets, the effortful-swallowing group completed a mean of 14.3 exercise units per week (range = 9.5 – 15). The modified head-lift manoeuvre group completed a mean of 14.2 exercise units per week (range = 12 – 15). The mean length of time taken to complete each exercise unit was 11.4 min for the effortful-swallowing group (range = 5 – 20) and 6.9 min for the modified head-lift group (range = 3 – 12).

For the modified head-lift manoeuvre, participants were asked to record how long they could hold the sustained head-lift for at each exercise unit. The mean duration of sustained lift was 29.6 s (range = 15 – 40).

### 13.3 Corticobulbar excitability results

Of the 20 participants assigned to the effortful-swallowing group, 15 had recordable MEPs during volitional contraction of the submental muscles, and 14 of these also had recordable MEPs during volitional swallowing. Of the 21 participants assigned to the modified head-lift group, 19 had recordable MEPs during volitional contraction of the submental muscles, and 17 of these also had recordable MEPs during volitional swallowing.

Raw data plots for MEP area and onset latency recorded during both volitional contraction and swallowing are provided in Appendix VI.

### 13.3.1 Submental MEPs recorded during volitional contraction

#### 13.3.1.1 Short-term effects

Mean area for the baseline and following four time points from the raw data are presented in Figure 13.1 for both the effortful-swallowing group and the modified head-lift group. Intervals represent 95% confidence around the means. The standard deviations were 1364  $\mu\text{V}\cdot\text{ms}$  (58%) across participants and 810  $\mu\text{V}\cdot\text{ms}$  (34%) within participants for the effortful-swallowing group, and 929  $\mu\text{V}\cdot\text{ms}$  (46%) and 683  $\mu\text{V}\cdot\text{ms}$  (34%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group for any time point immediately following the first exercise session, with all estimated effects having a 95% confidence interval that includes zero. The estimated effects are provided as a percentage of the mean in Table 13.1, with 95% confidence intervals and  $p$ -values. A negative value represents a decrease and a positive value represents an increase.

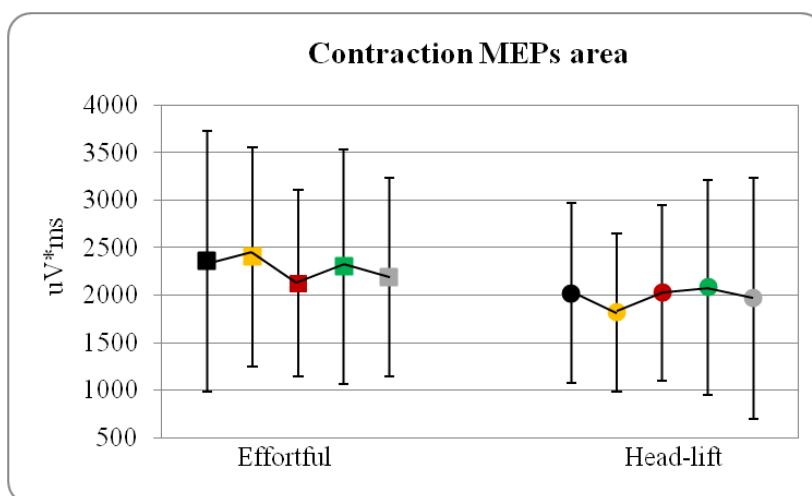


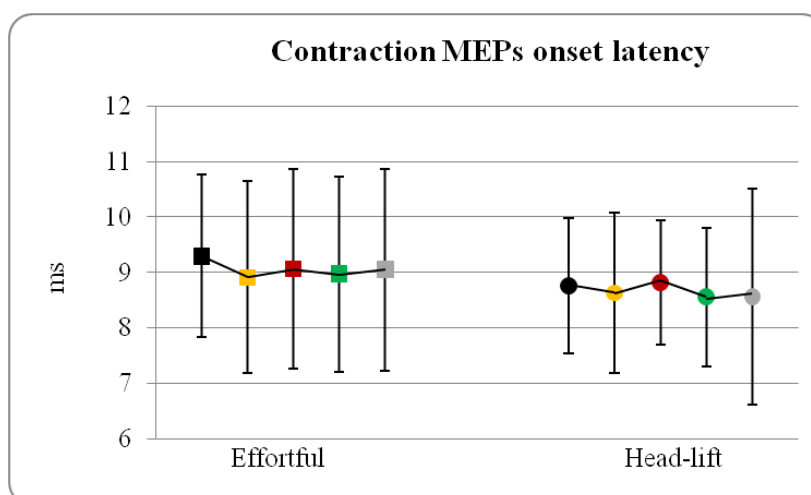
Figure 13.1. Group means of volitional contraction MEP area for both the effortful-swallowing and modified head-lift group at the baseline session and four time points after the first exercise session. The error bars represent  $\pm 1$  standard deviation of the group mean. Black = baseline session, yellow = <5 min post the first exercise session, red = 30 min post the first exercise session, green = 60 min post the first exercise session, grey = 90 min post the first exercise session.

Mean onset latencies for the baseline and following four time points from the raw data are presented in Figure 13.2 for both groups. The standard deviations were 1.4 ms (15%) across participants and 1.0 ms (11%) within participants for the effortful-swallowing group, and 1.1

ms (13%) and 1.0 ms (11%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group for any time point immediately following the first exercise session. The estimated effects, 95% confidence intervals, and  $p$ -values are provided Table 13.2.

**Table 13.1. Estimated effects of one exercise session on area of MEPs recorded during volitional contraction at <5 min, 30 min, 60 min and 90 min following completion of the first exercise session. Lower and upper limits represent 95% confidence intervals of estimated effects.**

Time point	Effortful-swallowing group				Modified head-lift group			
	Lower	Estimate	Upper	$p$	Lower	Estimate	Upper	$p$
<b>5min</b>	-11%	2%	15%	0.76	-22%	-10%	2%	0.10
<b>30min</b>	-35%	-10%	15%	0.42	-11%	0%	12%	0.98
<b>60min</b>	-17%	-2%	12%	0.73	-18%	3%	24%	0.78
<b>90min</b>	-28%	-7%	14%	0.50	-26%	-3%	21%	0.82



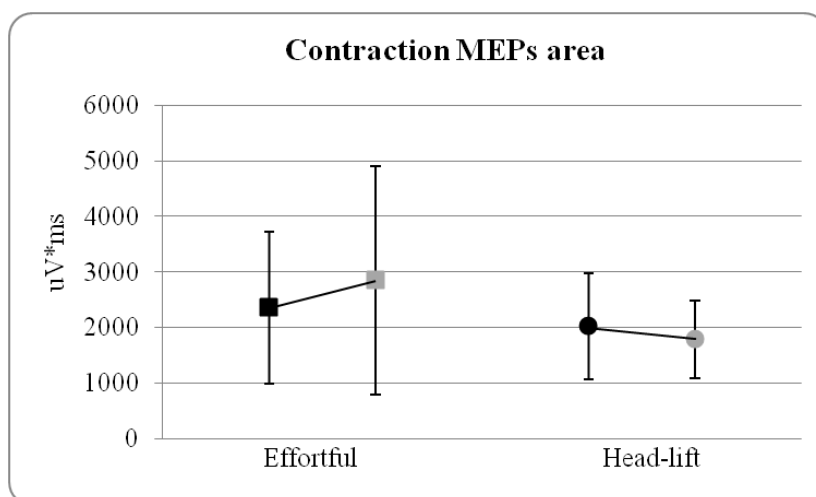
*Figure 13.2. Group means and standard deviations of volitional contraction MEP onset latencies following the first exercise session for both the effortful-swallowing and modified head-lift group.*

**Table 13.2. Estimated effects of one exercise session on MEP onset latencies recorded during volitional contraction at <5, 30, 60 and 90 min following completion of the first exercise session.**

Time point	Effortful-swallowing group				Modified head-lift group			
	Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
<b>5min</b>	-11%	4%	3%	0.24	-7%	-1%	3%	0.57
<b>30min</b>	-8%	-2%	3%	0.37	-6%	1%	7%	0.82
<b>60min</b>	-10%	-2%	2%	0.23	-8%	-2%	3%	0.43
<b>90min</b>	-10%	-2%	4%	0.44	-9%	-2%	6%	0.57

### 13.3.1.2 Cumulative effects

Mean area for the baseline and outcome sessions are presented in Figure 13.3 for both groups. The standard deviations were 1209  $\mu\text{V}\cdot\text{ms}$  (51%) across participants and 1698  $\mu\text{V}\cdot\text{ms}$  (72%) within participants for the effortful-swallowing group, and 892  $\mu\text{V}\cdot\text{ms}$  (44%) and 672  $\mu\text{V}\cdot\text{ms}$  (33%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.3.

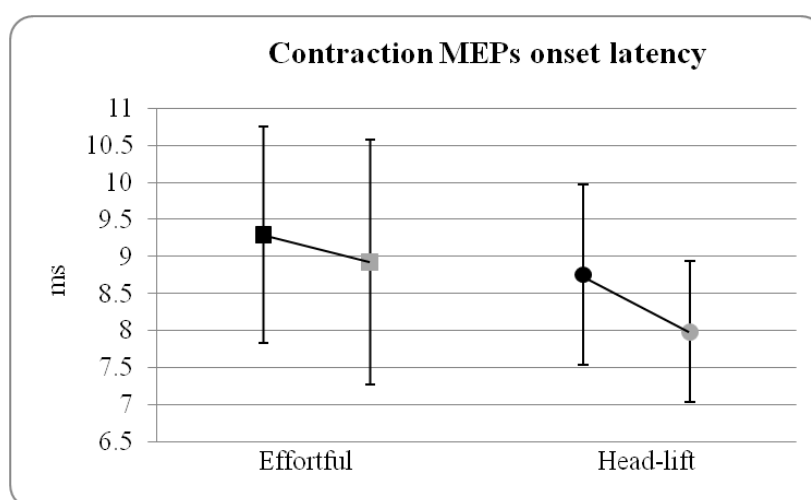


*Figure 13.3. Group means and standard deviations of volitional contraction MEP area at baseline and following 6 weeks of exercise for both the effortful-swallowing and modified head-lift group.*

**Table 13.3. Estimated effects of six weeks of exercise on area of MEPs recorded during volitional contraction.**

Time point	Effortful-swallowing group				Modified head-lift group			
	Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
5min	-24%	21%	66%	0.34	-31%	-12%	8%	0.22

Mean onset latencies for the baseline and outcome sessions are presented in Figure 13.4 for both groups. The standard deviations were 1.4 ms (15%) across participants and .9 ms (10%) within participants for the effortful-swallowing group, and 1.1 ms (13%) and 1.4 ms (16%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing group following six weeks of exercise. While the Bonferroni-corrected level of significance indicates the effect of the modified head-lift manoeuvre on volitional contraction MEP latency is not statistically significant, the confidence interval around the estimated effect does not include zero, suggesting evidence of an effect. The estimated effect is a decrease in onset latency following treatment. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.4.



*Figure 13.4. Group means and standard deviations of volitional contraction MEP onset latencies for both the effortful-swallowing and modified head-lift group.*

**Table 13.4. Estimated effects of six weeks of exercise on MEP onset latencies recorded during volitional contraction.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-11%	-4%	3%	0.23	-17%	-9%	-0.3%	0.04

### 13.3.2 Submental MEPs recorded during volitional swallowing

#### 13.3.2.1 Short-term effects

Mean area for the baseline and following four time points are presented in Figure 13.5 for both the effortful-swallowing group and the modified head-lift group. Intervals represent 95% confidence around the means. The standard deviations were 1272  $\mu\text{V}\cdot\text{ms}$  (72%) across participants and 544  $\mu\text{V}\cdot\text{ms}$  (31%) within participants for the effortful-swallowing group, and 731  $\mu\text{V}\cdot\text{ms}$  (43%) and 416  $\mu\text{V}\cdot\text{ms}$  (24%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group for any time point immediately following the first exercise session. The estimated effects, 95% confidence intervals, and *p*-values are provided in Table 13.5.

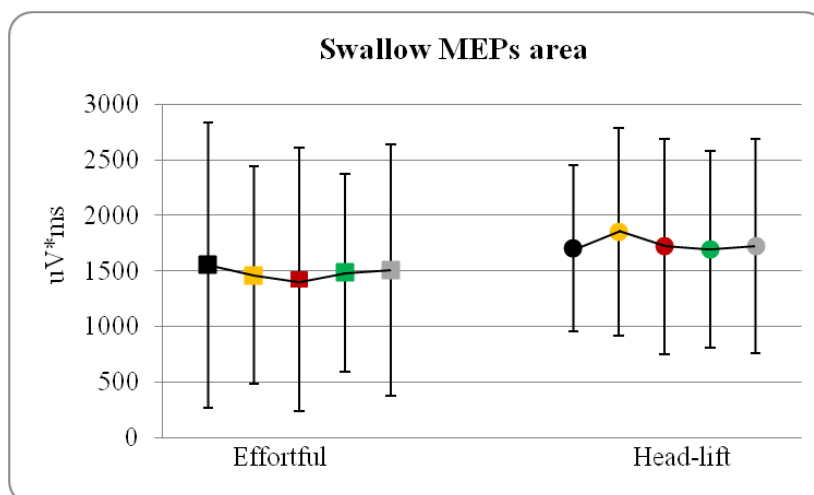


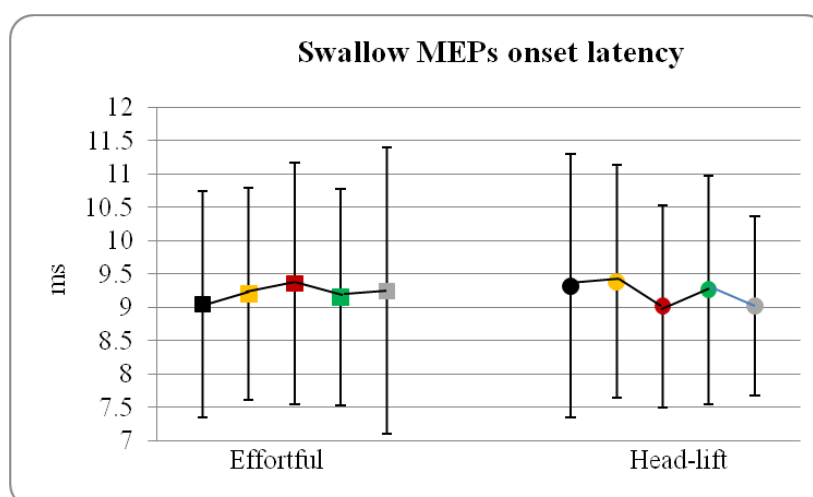
Figure 13.5. Group means and standard deviations of volitional swallowing MEP area for the baseline session and four time points following the first exercise session for both the effortful-swallowing and modified head-lift group.



**Table 13.5. Estimated effects of one exercise session on MEP area recorded during volitional swallowing at <5, 30, 60 and 90 min following completion of the first exercise session.**

Time point	Effortful-swallowing group				Modified head-lift group			
	Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
<b>5min</b>	-21%	-9%	4%	0.18	-6%	8%	23%	0.23
<b>30min</b>	-23%	-4%	15%	0.66	-14%	1%	16%	0.90
<b>60min</b>	-36%	-7%	22%	0.64	-12%	-1%	10%	0.92
<b>90min</b>	-15%	-3%	10%	0.65	-12%	10%	14%	0.88

Mean onset latencies for the baseline and following four time points are presented in Figure 13.6 for both the effortful-swallowing group and the modified head-lift group. Intervals represent 95% confidence around the means. The standard deviations were 1.6 ms (18%) across participants and 1.4 ms (15%) within participants for the effortful-swallowing group, and 1.9 ms (21%) and 0.2 ms (2%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group for any time point immediately following the first exercise session. The estimated effects, 95% confidence intervals, and *p*-values are provided in Table 13.6.



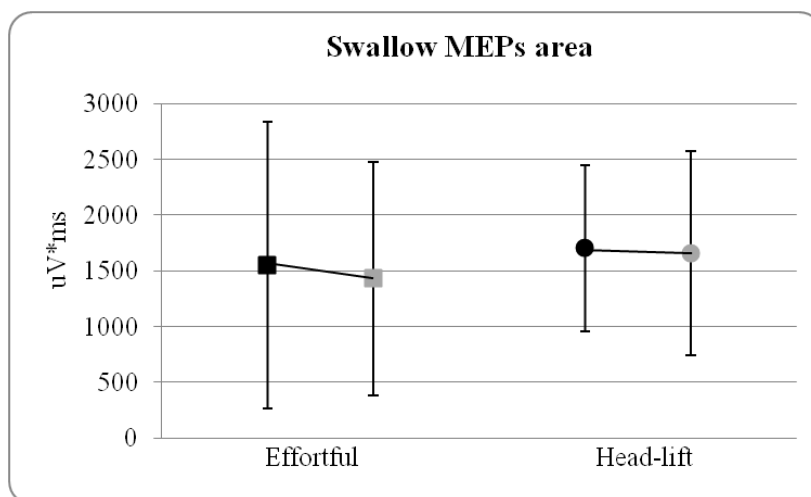
*Figure 13.6. Group means and standard deviations of volitional swallowing MEP onset latencies at the baseline and four time points following the first exercise session for both the effortful-swallowing and modified head-lift group.*

**Table 13.6. Estimated effects of one exercise session on MEP onset latencies recorded during volitional swallowing at <5, 30, 60 and 90 min following completion of the first exercise session.**

Time point	Effortful-swallowing group				Modified head-lift group			
	Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
<b>5min</b>	-6%	2%	9%	0.64	-4%	1%	6%	0.79
<b>30min</b>	-6%	3%	13%	0.47	-6%	-3%	2%	0.23
<b>60min</b>	-8%	1%	10%	0.80	-9%	-1%	4%	0.83
<b>90min</b>	-7%	2%	11%	0.63	-11%	-3%	4%	0.42

### 13.3.2.2 Cumulative effects

Mean area for the baseline and outcome sessions are presented in Figure 13.7 for both groups. The standard deviations were 1221  $\mu\text{V}\cdot\text{ms}$  (69%) across participants and 660  $\mu\text{V}\cdot\text{ms}$  (37%) within participants for the effortful-swallowing group, and 679  $\mu\text{V}\cdot\text{ms}$  (40%) and 685  $\mu\text{V}\cdot\text{ms}$  (40%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.7.



*Figure 13.7. Group means and standard deviations of volitional swallowing MEP area at the baseline session and following 6 weeks of exercise for both the effortful-swallowing and modified head-lift group.*

**Table 13.7. Estimated effects of six weeks of exercise on MEP area recorded during volitional swallowing.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-36%	-8%	21%	0.57	-27%	-3%	22%	0.82

Mean onset latencies for the baseline and outcome sessions are presented in Figure 13.8 for both groups. The standard deviations were 1.6 ms (18%) across participants and 1.5 ms (16%) within participants for the effortful-swallowing group, and 1.9 ms (20%) and 1.3 ms (14%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.8.

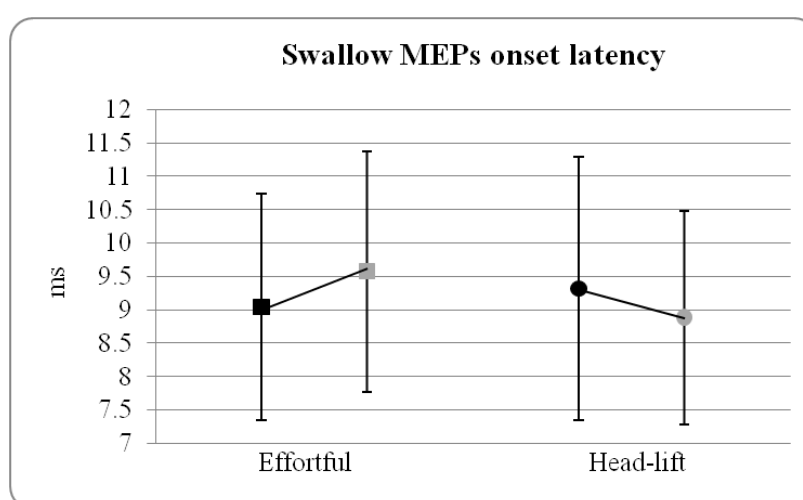


Figure 13.8. Group means and standard deviations of volitional swallowing MEP onset latencies for both the effortful-swallowing and modified head-lift group.

**Table 13.8. Estimated effects of six weeks of exercise on MEP onset latencies recorded during volitional swallowing.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-6%	6%	17%	0.28	-14%	-4%	3%	0.28

## 13.4 Pharyngeal pressure results

Of the 20 people assigned to the effortful-swallowing group, manometric data were not collected from 2 participants due to intolerance of catheter placement or unusable data. Of the 21 people assigned to the modified head-lift group manometric data were not obtained from 3 participants due to intolerance of catheter placement or unusable data.

Raw data plots for pharyngeal pressure amplitudes and durations for both exercise groups during dry, effortful, and 10 mL water swallows are presented in Appendix VI.

### 13.4.1 Pharyngeal pressures during dry swallows

#### 13.4.1.1 Upper pharynx (sensor 1)

Mean amplitudes for the baseline and outcome sessions are presented in Figure 13.9 for both groups. The standard deviations were 30 mmHg (30%) across participants and 30 mmHg (30%) within participants for the effortful-swallowing group, and 39 mmHg (36%) and 38 mmHg (35%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and  $p$ -values are provided Table 13.9.

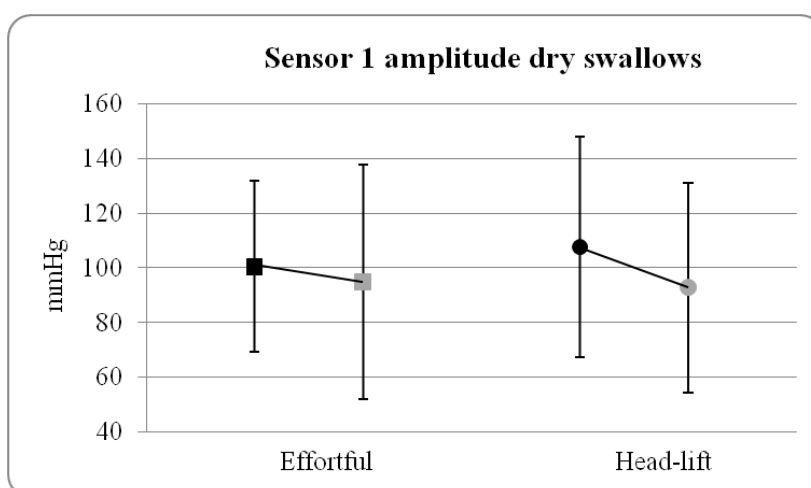


Figure 13.9. Group means and standard deviations of amplitude of upper pharyngeal pressures during dry swallows for both the effortful-swallowing and modified head-lift group.

**Table 13.9. Estimated effects of six weeks of exercise on upper-pharyngeal pressure amplitudes recorded during dry swallowing.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-21%	-6%	9%	0.46	-31%	-14%	4%	0.11

Mean durations for the baseline and outcome sessions are presented in Figure 13.10 for both groups. The standard deviations were .112 s (21%) across participants and .125 s (23%) within participants for the effortful-swallowing group, and .126 s (24%) and .088 s (17%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.9.

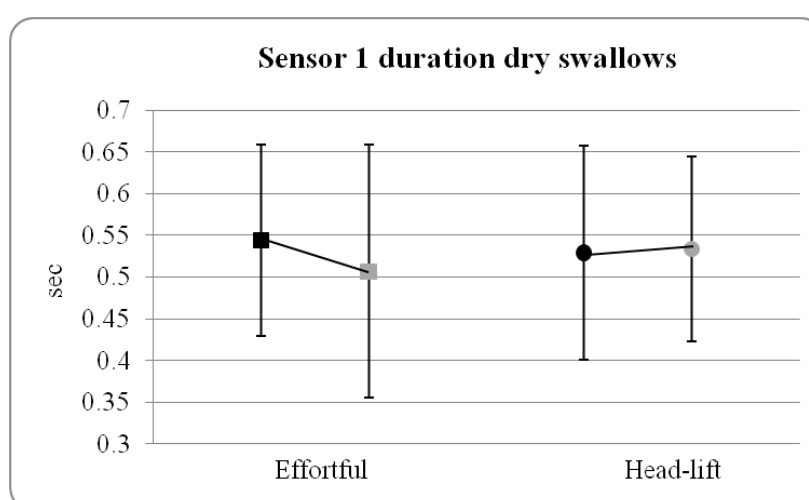


Figure 13.10. Group means and standard deviations of duration of upper pharyngeal pressures during dry swallowing for both the effortful-swallowing and modified head-lift group.

**Table 13.10. Estimated effects of six weeks of exercise on upper-pharyngeal pressure durations recorded during dry swallowing.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-18%	-7%	4%	0.22	-7%	1%	9%	0.82

### 13.4.1.2 Hypopharynx (sensor 2)

Mean amplitudes for the baseline and outcome sessions are presented in Figure 13.11 for both groups. The standard deviations were 58 mmHg (45%) across participants and 45 mmHg (35%) within participants for the effortful-swallowing group, and 49 mmHg (48%) and 38 mmHg (37%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and  $p$ -values are provided Table 13.11.

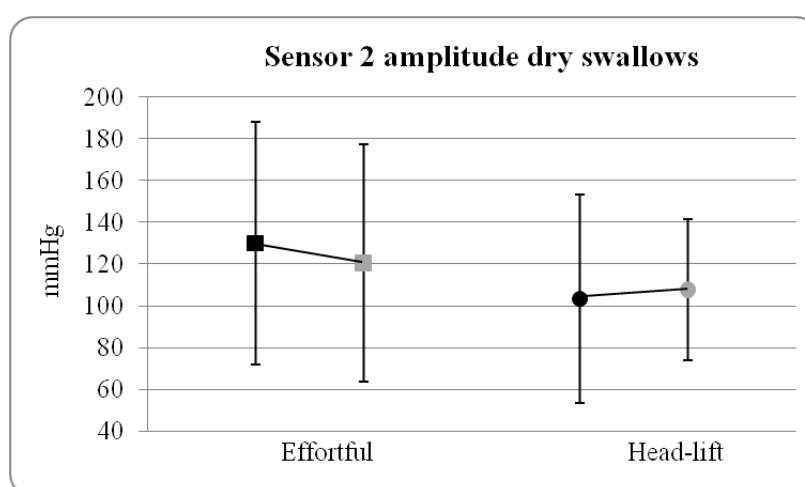


Figure 13.11. Group means and standard deviations of amplitude of hypopharyngeal pressures during dry swallows for both the effortful-swallowing and modified head-lift group.

**Table 13.11. Estimated effects of six weeks of exercise on hypo-pharyngeal pressure amplitudes recorded during dry swallowing.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	$p$	Lower	Estimate	Upper	$p$
-24%	-8%	9%	0.38	-14%	4%	21%	0.64

Mean durations for the baseline and outcome sessions are presented in Figure 13.12 for both groups. The standard deviations were .129 s (34%) across participants and .196 s (51%) within participants for the effortful-swallowing group, and .086 s (18%) and .100 s (23%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and  $p$ -values are provided Table 13.12.

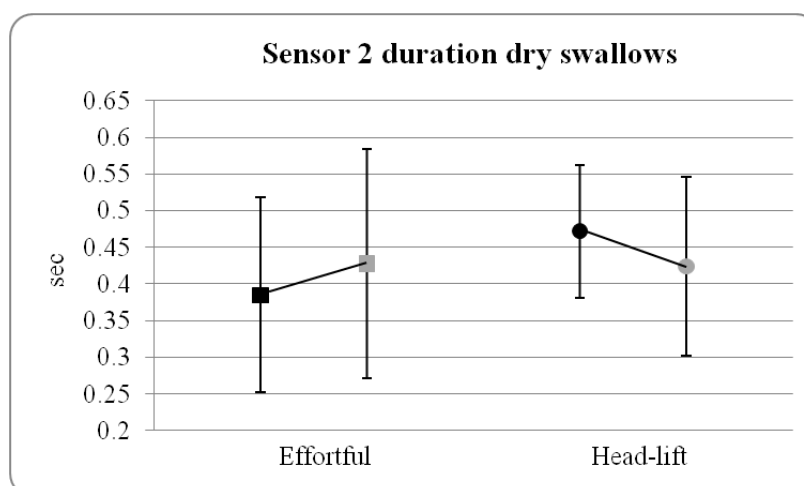


Figure 13.12. Group means and standard deviations of duration of hypopharyngeal pressures during dry swallows for both the effortful-swallowing and modified head-lift group.

Table 13.12. Estimated effects of six weeks of exercise on hypo-pharyngeal pressure durations recorded during dry swallowing.

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-13%	11%	35%	0.37	-21%	-10%	0%	0.06

### 13.4.1.3 UES (sensor 3)

Mean amplitudes for the baseline and outcome sessions are presented in Figure 13.13 for both groups. The standard deviations were 6 mmHg (75%) across participants and 5 mmHg (63%) within participants for the effortful-swallowing group, and 5 mmHg (56%) and 6 mmHg (67%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.13.

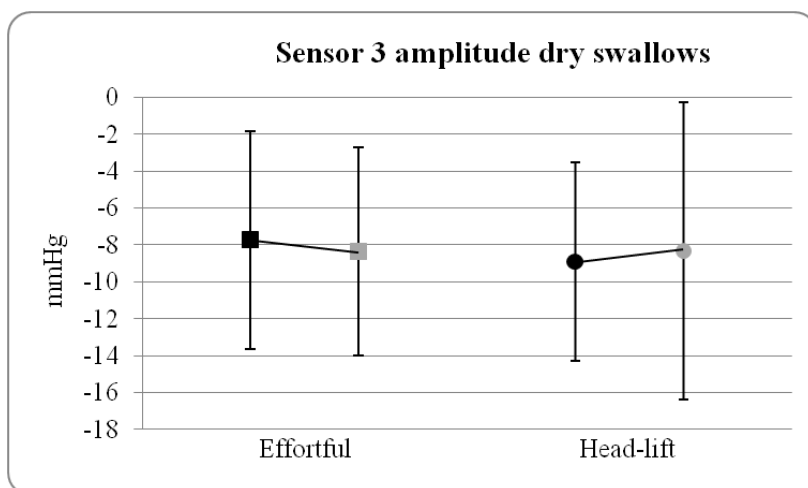


Figure 13.13. Group means and standard deviations of nadir amplitude of UES pressures during dry swallows for both the effortful-swallowing and modified head-lift group

**Table 13.13. Estimated effects of six weeks of exercise on UES nadir pressure amplitudes recorded during dry swallowing.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-38%	-1%	25%	0.63	-22%	11%	44%	0.70

Mean durations for the baseline and outcome sessions are presented in Figure 13.14 for both groups. The standard deviations were .207 s (24%) across participants and .238 s (27%) within participants for the effortful-swallowing group, and .186 s (22%) and .131 s (15%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.14.



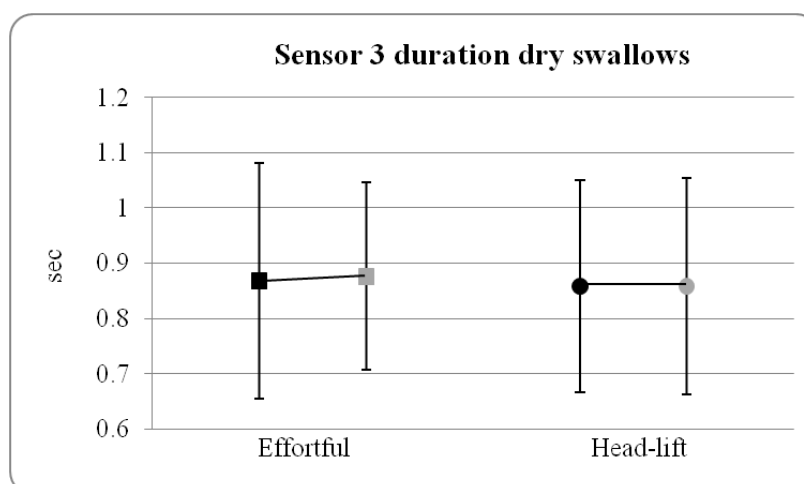


Figure 13.14. Group means and standard deviations of duration of UES pressures during dry swallows for both the effortful-swallowing and modified head-lift group.

**Table 13.14. Estimated effects of six weeks of exercise on UES pressure durations recorded during dry swallowing.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-12%	1%	14%	0.88	-8%	0%	8%	0.99

#### ***13.4.1.4 Time from peak pressure in upper pharynx to peak pressure in hypopharynx***

Mean durations for the baseline and outcome sessions are presented in Figure 13.15 for both groups. The standard deviations were .111 s (60%) across participants and .111 s (60%) within participants for the effortful-swallowing group, and .107 s (79%) and .114 s (84%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.15.

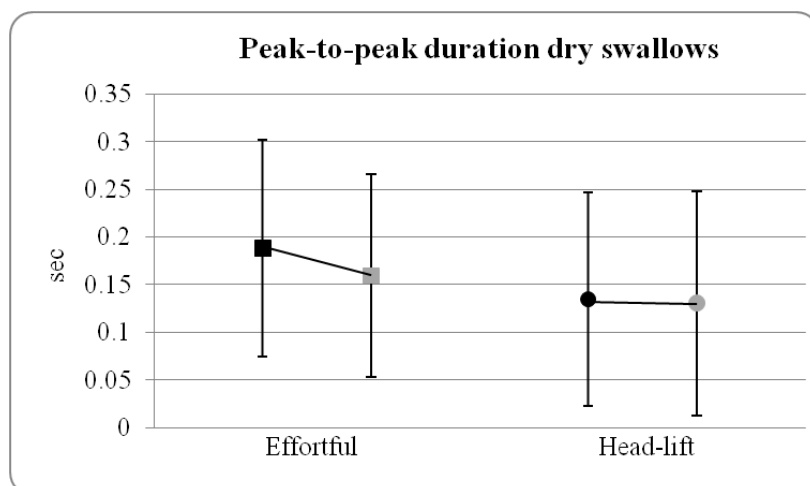


Figure 13.15. Group means and standard deviations of the duration between peak pressure in the upper pharynx and peak pressure in the hypopharynx during dry swallows for both the effortful-swallowing and modified head-lift group.

**Table 13.15. Estimated effects of six weeks of exercise on the duration between peak pressure in the upper pharynx and peak pressure in the hypopharynx recorded during dry swallowing.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-44%	-15%	14%	0.31	-46%	-3%	39%	0.88

#### 13.4.1.5 Total duration of swallowing

Mean durations for the baseline and outcome sessions are presented in Figure 13.16 for both groups. The standard deviations were .190 s (21%) across participants and .215 s (24%) within participants for the effortful-swallowing group, and .162 s (18%) and .107 s (12%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.16.

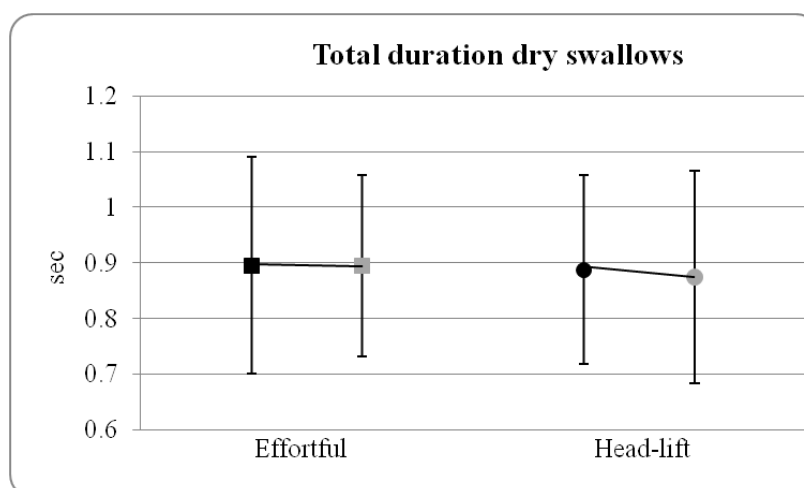


Figure 13.16. Group means and standard deviations of the total duration of swallowing pressures during dry swallows for both the effortful-swallowing and modified head-lift group.

**Table 13.16. Estimated effects of six weeks of exercise on the total swallowing duration recorded during dry swallowing.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-12%	0%	12%	1.00	-8%	-1%	5%	0.68

## 13.4.2 Pharyngeal pressures during effortful swallows

### 13.4.2.1 Upper pharynx (sensor 1)

Mean amplitudes for the baseline and outcome sessions are presented in Figure 13.17 for both groups. The standard deviations were 30 mmHg (27%) across participants and 40 mmHg (36%) within participants for the effortful-swallowing group, and 43 mmHg (36%) and 27 mmHg (23%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing group following six weeks of exercise. While Bonferroni correction suggests the effect of six weeks of modified head-lift manoeuvre on upper-pharyngeal pressure amplitude is not significant, the 95% confidence intervals around the estimated effect do not include zero, suggesting evidence of an effect. The estimated effects suggest there was a decrease in upper-pharyngeal pressures during effortful-swallowing following six weeks of modified head-lift exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.17.

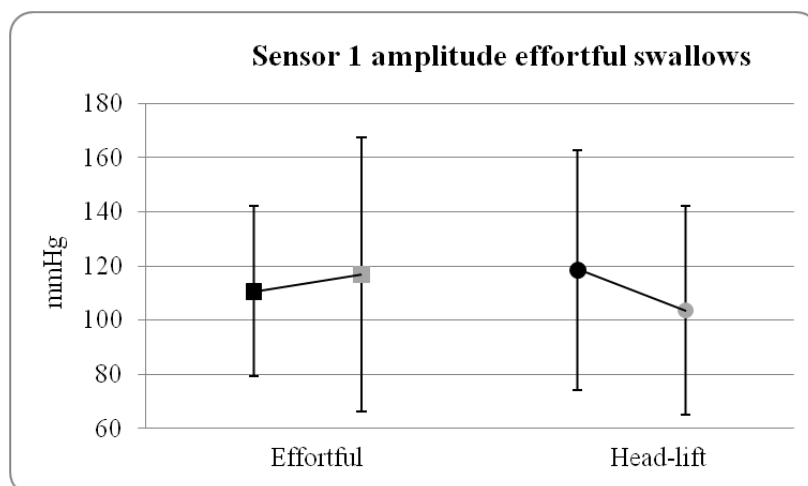


Figure 13.17. Group means and standard deviations of amplitude of upper pharyngeal pressures during effortful swallows for both the effortful-swallowing and modified head-lift group.

**Table 13.17. Estimated effects of six weeks of exercise on upper-pharyngeal pressure amplitudes recorded during effortful-swallowing.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-13%	5%	23%	0.54	-25%	-13%	-1%	0.04

Mean durations for the baseline and outcome sessions are presented in Figure 13.18 for both groups. The standard deviations were .118 (18%) s across participants and .107 s (17%) within participants for the effortful-swallowing group, and .169 s (27%) and .121 s (19%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.18.

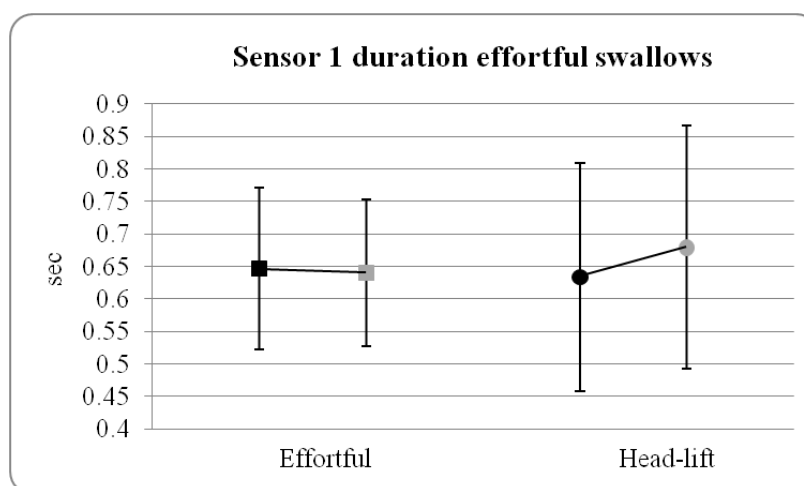


Figure 13.18. Group means and standard deviations of duration of upper pharyngeal pressures during effortful swallows for both the effortful-swallowing and modified head-lift group.

**Table 13.18. Estimated effects of six weeks of exercise on upper-pharyngeal pressure durations recorded during effortful-swallowing.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-10%	-1%	8%	0.81	-3%	7%	18%	0.17

#### 13.4.2.2 Hypopharynx (sensor 2)

Mean amplitudes for the baseline and outcome sessions are presented in Figure 13.19 for both groups. The standard deviations were 59 mmHg (39%) across participants and 72 mmHg (47%) within participants for the effortful-swallowing group, and 32 mmHg (30%) and 24 mmHg (23%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.19.

Mean durations for the baseline and outcome sessions are presented in Figure 13.20 for both groups. The standard deviations were .093 s (17%) across participants and .128 s (23%) within participants for the effortful-swallowing group, and .173 s (29%) and .225 s (38%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.20.

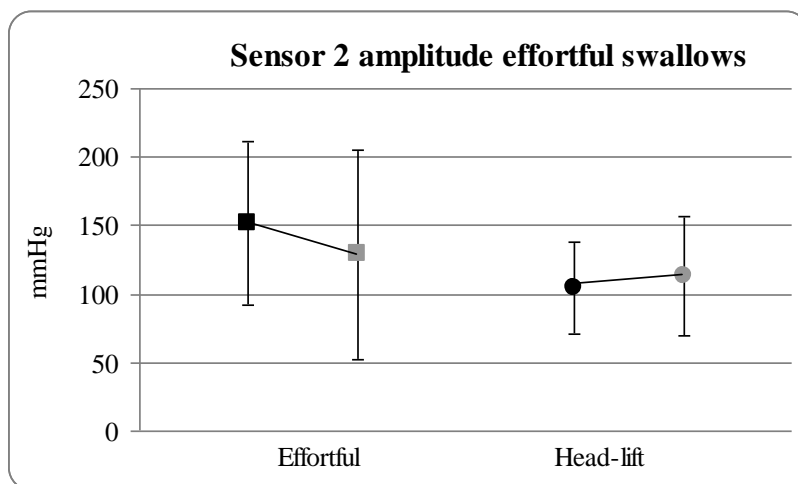


Figure 13.19. Group means and standard deviations of amplitude of hypopharyngeal pressures during effortful swallows for both the effortful-swallowing and modified head-lift group.

**Table 13.19. Estimated effects of six weeks of exercise on hypo-pharyngeal pressure amplitudes recorded during effortful-swallowing.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-38%	-15%	8%	0.20	-4%	9%	20%	0.18

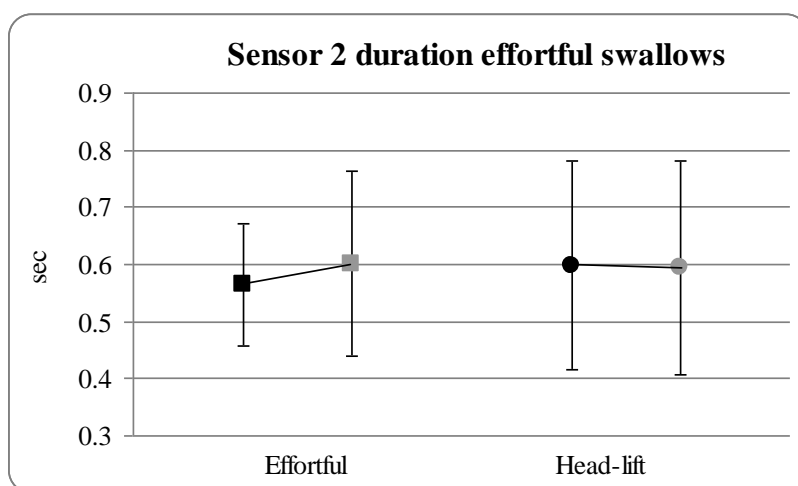


Figure 13.20. Group means and standard deviations of duration of hypopharyngeal pressures during effortful swallows for both the effortful-swallowing and modified head-lift group.

**Table 13.20. Estimated effects of six weeks of exercise on upper-pharyngeal pressure durations recorded during effortful-swallowing.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-6%	7%	19%	0.29	-20%	-1%	19%	0.96

### 13.4.2.3 UES (sensor 3)

Mean amplitudes for the baseline and outcome sessions are presented in Figure 13.21 for both groups. The standard deviations were 7 mmHg (70%) across participants and 7 mmHg (70%) within participants for the effortful-swallowing group, and 6 mmHg (75%) and 4 mmHg (50%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.21.

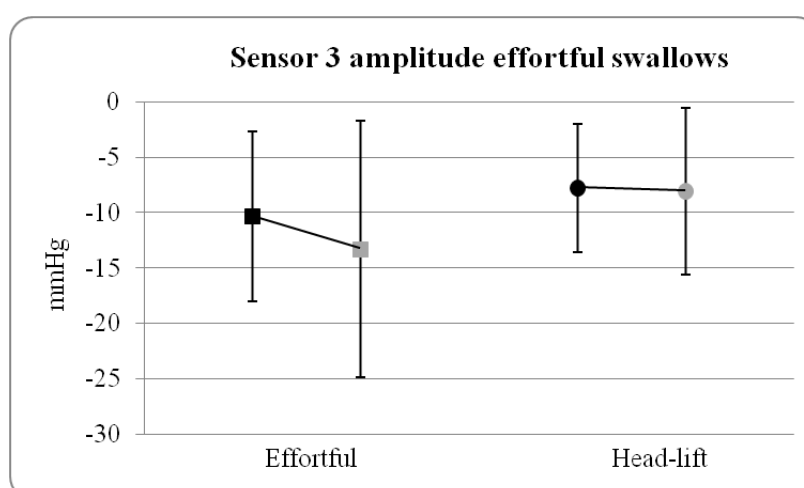


Figure 13.21. Group means and standard deviations of nadir amplitudes of UES pressures during effortful swallows for both the effortful-swallowing and modified head-lift group.

**Table 13.21. Estimated effects of six weeks of exercise on UES nadir pressure amplitudes recorded during effortful-swallowing.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-70%	-30%	10%	0.10	-25%	0%	25%	0.82

Mean durations for the baseline and outcome sessions are presented in Figure 13.22 for both groups. The standard deviations were .163 s (18%) across participants and .328 s (36%) within participants for the effortful-swallowing group, and .272 s (28%) and .310 s (32%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and  $p$ -values are provided Table 13.22.

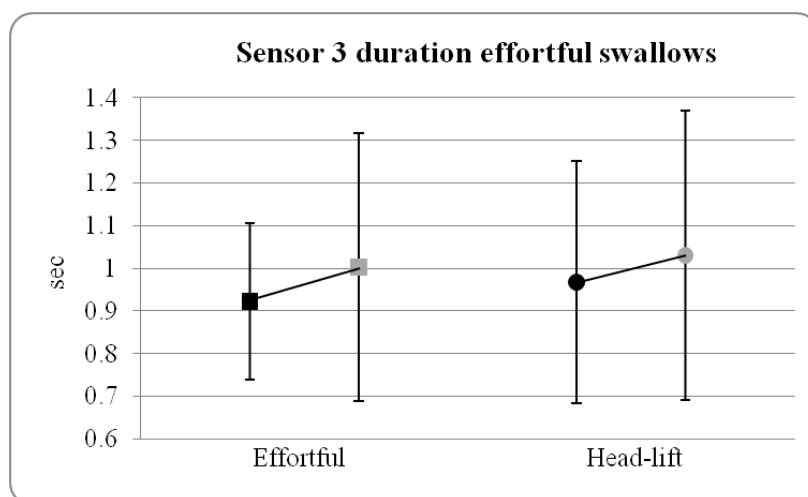


Figure 13.22. Group means and standard deviations of duration of UES pressures during effortful-swallowing for both the effortful-swallowing and modified head-lift group.

**Table 13.22. Estimated effects of six weeks of exercise on UES pressure durations recorded during effortful-swallowing.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	$p$	Lower	Estimate	Upper	$p$
-9%	9%	26%	0.33	-9%	7%	22%	0.41

#### 13.4.2.4 Time from peak pressure in upper pharynx to peak pressure in hypopharynx

Mean durations for the baseline and outcome sessions are presented in Figure 13.23 for both groups. The standard deviations were .093 s (46%) across participants and .142 s (70%) within participants for the effortful-swallowing group, and .092 s (71%) and .077 s (59%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-



swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.23.

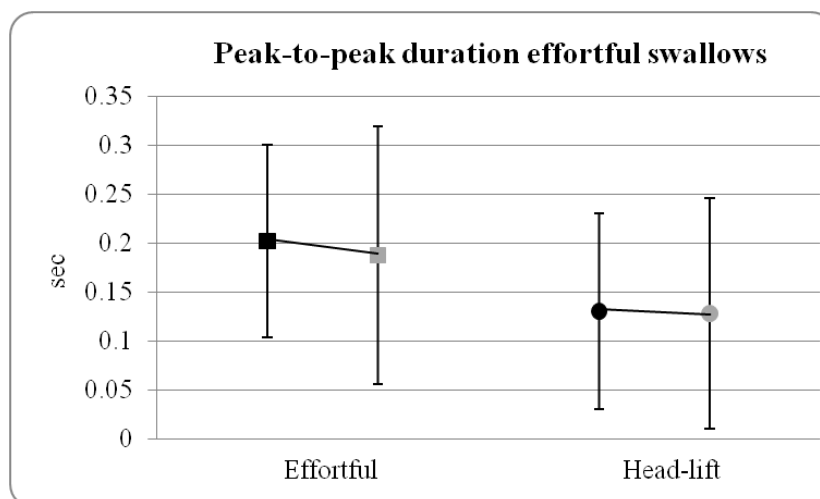


Figure 13.23. Group means and standard deviations of the duration between peak pressure in the upper pharynx and peak pressure in the hypopharynx during effortful-swallowing for both the effortful-swallowing and modified head-lift group.

**Table 13.15. Estimated effects of six weeks of exercise on the duration between peak pressure in the upper pharynx and peak pressure in the hypopharynx recorded during effortful-swallowing.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-42%	-7%	27%	0.68	-36%	-2%	32%	0.91

#### 13.4.2.5 Total duration of swallowing

Mean durations for the baseline and outcome sessions are presented in Figure 13.24 for both groups. The standard deviations were .137 s (14%) across participants and .315 s (33%) within participants for the effortful-swallowing group, and .222 s (22%) and .243 s (24%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.24.

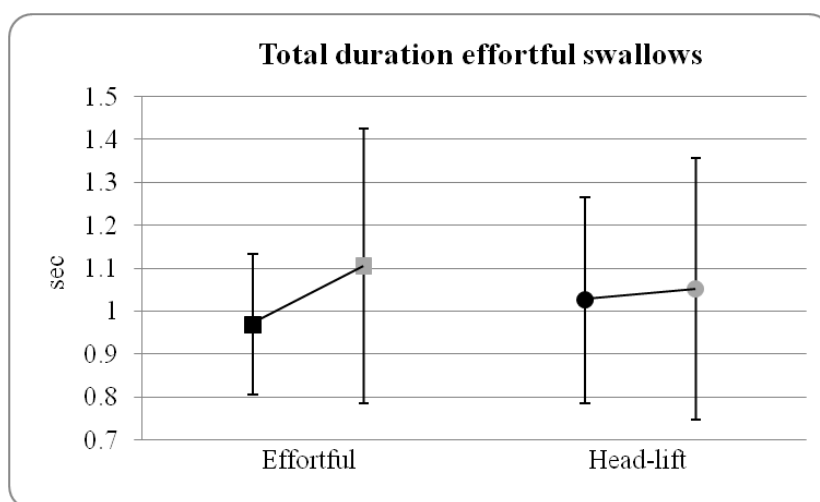


Figure 13.24. Group means and standard deviations of the total duration of swallowing pressures during effortful-swallowing for both the effortful-swallowing and modified head-lift group.

**Table 13.15. Estimated effects of six weeks of exercise on the total swallowing duration recorded during effortful-swallowing.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-2%	14%	30%	0.09	-10%	3%	15%	0.69

### 13.4.3 Pharyngeal pressures during 10 mL water bolus swallows

#### 13.4.3.1 Upper pharynx (sensor 1)

Mean amplitudes for the baseline and outcome sessions are presented in Figure 13.25 for both groups. The standard deviations were 49 mmHg (47%) across participants and 42 mmHg (40%) within participants for the effortful-swallowing group, and 44 mmHg (42%) and 56 mmHg (54%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.25.

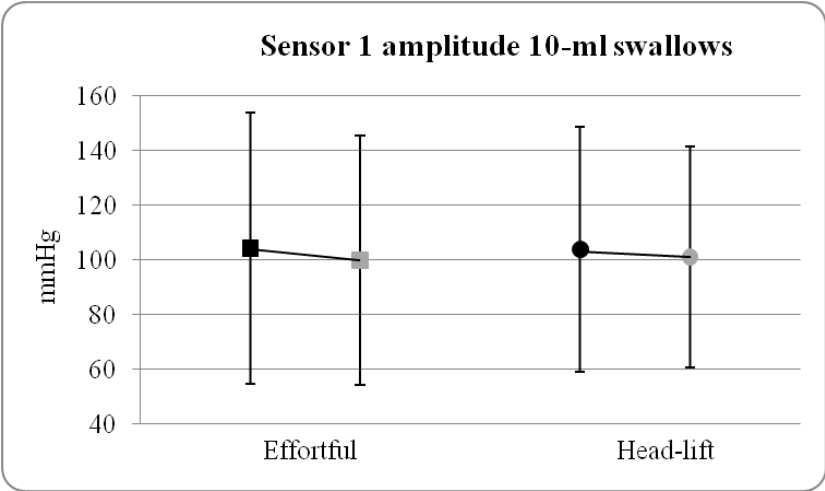


Figure 13.25. Group means and standard deviations of amplitude of upper pharyngeal pressures during 10 mL water swallows for both the effortful-swallowing and modified head-lift group.

Table 13.25. Estimated effects of six weeks of exercise on upper-pharyngeal pressure amplitudes recorded during 10 mL water swallows.

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-24%	-4%	15%	0.68	-29%	-3%	23%	0.83

Mean durations for the baseline and outcome sessions are presented in Figure 13.26 for both groups. The standard deviations were .118 s (26%) across participants and .094 s (21%) within participants for the effortful-swallowing group, and .146 s (34%) and .115 s (27%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.26.

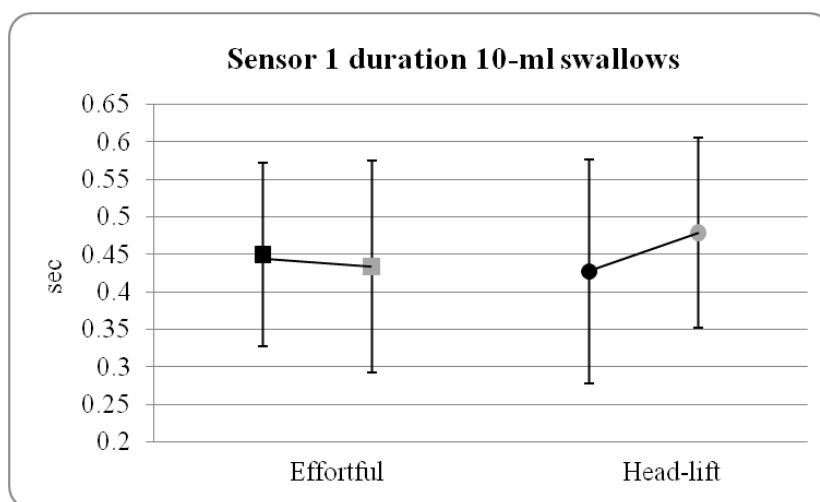


Figure 13.26. Group means and standard deviations of duration of upper pharyngeal pressures during 10 mL water swallows for both the effortful-swallowing and modified head-lift group.

**Table 13.26. Estimated effects of six weeks of exercise on upper-pharyngeal pressure durations recorded during 10 mL water swallows.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-14%	-4%	7%	0.52	-1%	12%	25%	0.07

#### 13.4.3.2 Hypopharynx (sensor 2)

Mean amplitudes for the baseline and outcome sessions are presented in Figure 13.27 for both groups. The standard deviations were 53 mmHg (40%) across participants and 56 mmHg (42%) within participants for the effortful-swallowing group, and 40 mmHg (39%) and 47 mmHg (46%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.27.

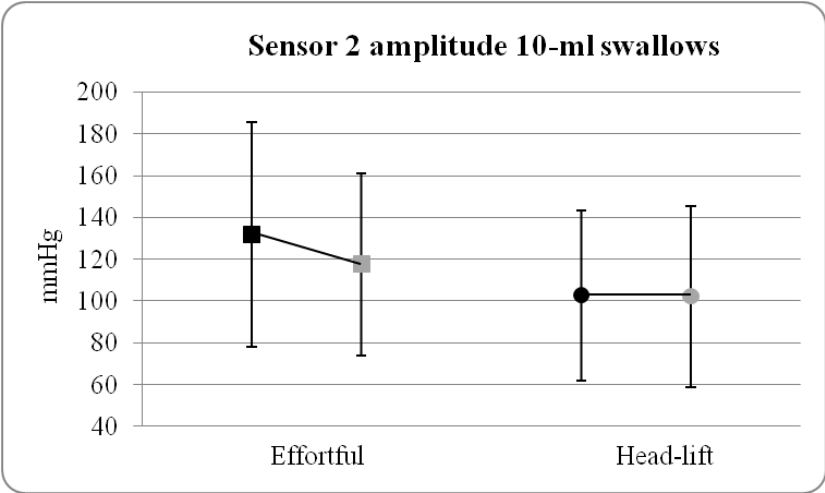


Figure 13.27. Group means and standard deviations of amplitude of hypopharyngeal pressures during 10 mL water swallows for both the effortful-swallowing and modified head-lift group.

Table 13.27. Estimated effects of six weeks of exercise on hypo-pharyngeal pressure amplitudes recorded during 10 mL water swallows.

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-31%	-11%	10%	0.30	-22%	0%	21%	0.97

Mean durations for the baseline and outcome sessions are presented in Figure 13.28 for both groups. The standard deviations were .076 s (25%) across participants and .086 s (28%) within participants for the effortful-swallowing group, and .105 s (29%) and .181 s (51%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.28.

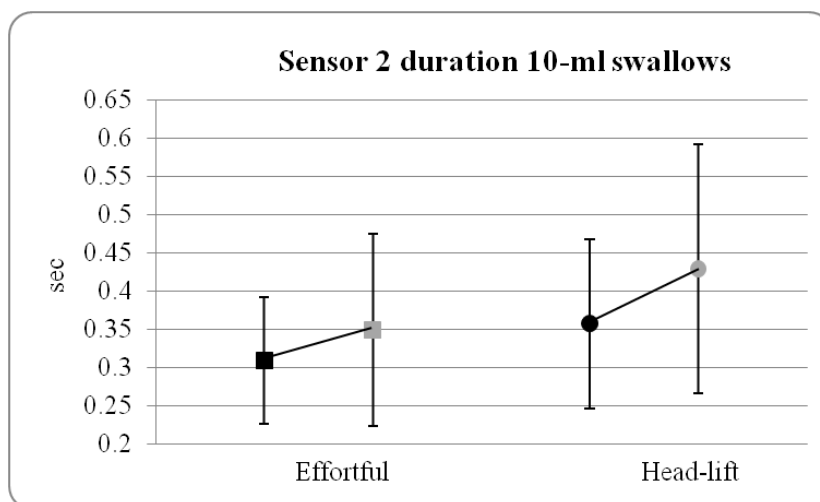


Figure 13.28. Group means and standard deviations of duration of hypopharyngeal pressures during 10 mL water swallows for both the effortful-swallowing and modified head-lift group.

**Table 13.28. Estimated effects of six weeks of exercise on hypo-pharyngeal pressure durations recorded during 10 mL water swallows.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-2%	13%	28%	0.08	-4%	20%	44%	0.11

### 13.4.3.3 UES (sensor 3)

Mean amplitudes for the baseline and outcome sessions are presented in Figure 13.29 for both groups. The standard deviations were 5 mmHg (83%) across participants and 4 mmHg (67%) within participants for the effortful-swallowing group, and 5 mmHg (100%) and 5 mmHg (100%) for the modified head-lift group. There was no evidence of an effect of treatment for the modified head-lift group following six weeks of exercise. While Bonferroni correction suggests the effects of effortful-swallowing exercise on UES pressures during 10 mL water swallowing is not significant, the confidence intervals around the estimated effect do not include zero, suggesting evidence of an effect. Estimated effects suggest a decrease in the magnitude of UES pressures following six weeks of effortful-swallowing exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.29. Note that while the effect of effortful-swallowing is represented as an increase, this actually reflects a decrease in magnitude of pressure amplitude, as increased magnitude of nadir pressures is optimal.

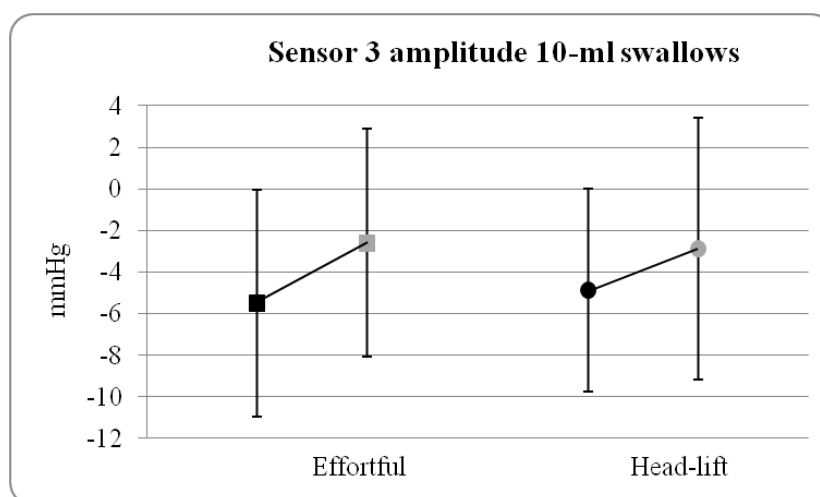


Figure 13.29. Group means and standard deviations of UES nadir amplitudes during 10 mL water swallows for both the effortful-swallowing and modified head-lift group.

**Table 13.29. Estimated effects of six weeks of exercise on UES nadir pressure amplitudes recorded during 10 mL water swallows.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
17%	50%	83%	0.01	-20%	40%	100%	0.12

Mean durations for the baseline and outcome sessions are presented in Figure 13.30 for both groups. The standard deviations were .217 s (24%) across participants and .283 s (31%) within participants for the effortful-swallowing group, and .263 s (26%) and .104 s (10%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.30.

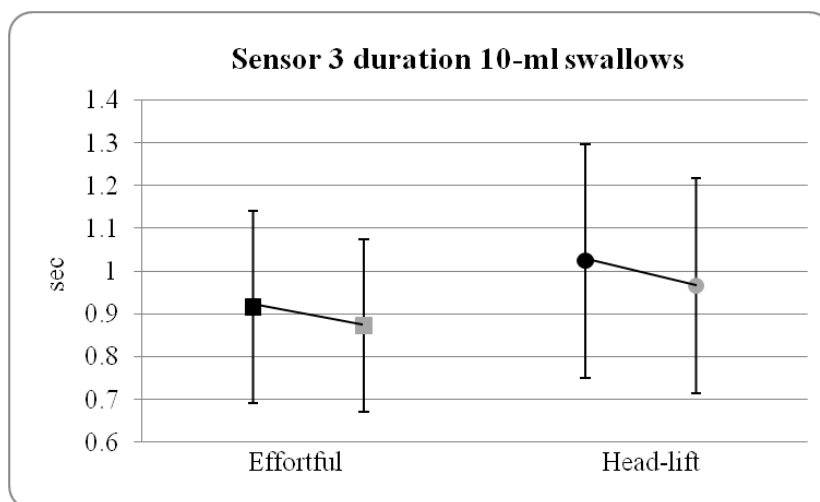


Figure 13.30. Group means and standard deviations of duration of UES pressures during 10 mL water swallows for both the effortful-swallowing and modified head-lift group.

**Table 13.30. Estimated effects of six weeks of exercise on UES pressure durations recorded during 10 mL water swallows.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-20%	-5%	10%	0.53	-12%	-6%	1%	0.09

#### 13.4.3.4 Time from peak pressure in upper pharynx to peak pressure in hypopharynx

Mean durations for the baseline and outcome sessions are presented in Figure 13.31 for both groups. The standard deviations were .107 s (55%) across participants and .127 s (66%) within participants for the effortful-swallowing group, and .117 s (71%) and .116 s (71%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.31.



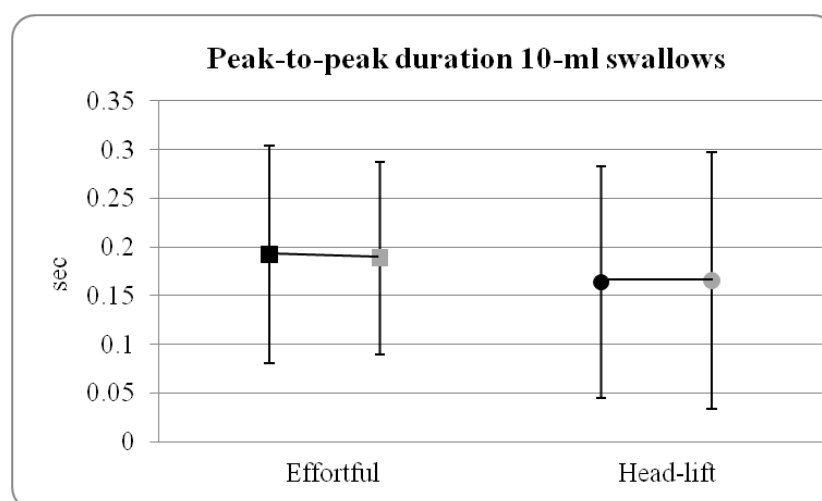


Figure 13.31. Group means and standard deviations of the duration between peak pressure in the upper pharynx and peak pressure in the hypopharynx during 10 mL water swallows for both the effortful-swallowing and modified head-lift group.

**Table 13.31. Estimated effects of six weeks of exercise on the duration between peak pressure in the upper pharynx and peak pressure in the hypopharynx recorded during 10 mL water swallows.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-35%	-2%	31%	0.90	-34%	1%	35%	0.97

#### 13.4.3.5 Total duration of swallowing

Mean durations for the baseline and outcome sessions are presented in Figure 13.32 for both groups. The standard deviations were .195 s (20%) across participants and .218 s (23%) within participants for the effortful-swallowing group, and .255 s (24%) and .113 s (11%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.32.

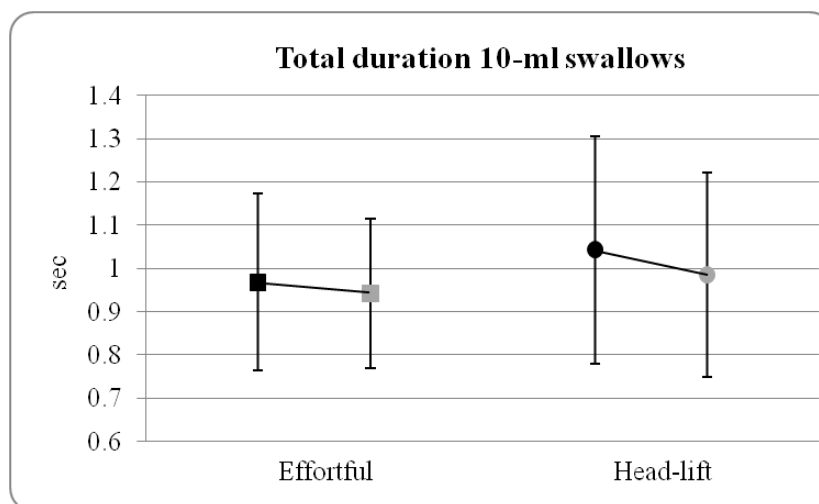


Figure 13.32. Group means and standard deviations of the total duration of swallowing pressures during 10 mL water swallows for both the effortful-swallowing and modified head-lift group.

**Table 13.32. Estimated effects of six weeks of exercise on the total swallowing durations recorded during 10 mL water swallows.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-14%	-3%	8%	0.63	-12%	-6%	1%	0.10

#### 13.4.4 Comparison of pharyngeal pressures during dry and effortful-swallowing

A comparison of pressure generation between dry and effortful swallows was completed to assess whether findings mimic those previously reported of increased pressure during execution of effortful swallows. Table 13.33 illustrates the effect of effortful-swallowing on pharyngeal pressures compared with dry swallows for each exercise group according to session. This reveals that at the baseline session, effortful-swallowing amplitudes were significantly greater than those of dry swallows for both the oropharynx and hypopharynx in the effortful-swallowing group. The UES pressures did not reach significance but demonstrated a trend towards increased magnitude of negative pressure during effortful-swallowing. For the outcome session, the difference between dry and effortful swallows was significant for the oropharynx but not significant for the hypopharynx. Also of interest are the baseline values for the modified head-lift group, which showed only the oropharynx had significantly different pressures for effortful versus non-effortful swallows. These results

suggest that (1) there was a difference at baseline between the two groups, (2) for the effortful-swallowing group, there were differences in oropharyngeal and hypopharyngeal pressures during the execution of the effortful-swallowing technique compared with dry swallows at baseline but only at the oropharynx after exercise, and (3) for the modified head-lift group there were differences in oropharyngeal pressures only both prior to and following the exercise.

**Table 13.33. Difference in pressures between dry and effortful swallows for each group across sessions. Intervals represent 95% confidence around the estimated effects.**

Exercise Group	Session	Sensor	Estimated effect	95% CI	<i>p</i> value
Effortful-swallowing	Baseline	1	↑ 12	[1,24]	0.04
		2	↑ 22	[3,40]	0.02
		3	↓ 2	[-5,0]	0.07
	Outcome	1	↑ 22	[3,41]	0.03
		2	↓ 3	[-24,18]	0.75
		3	↓ 5	[-10,0]	0.06
Modified head-lift manoeuvre	Baseline	1	↑ 9	[1,16]	0.03
		2	↑ 1	[-13,15]	0.84
		3	↑ 1	[-1,4]	0.26
	Outcome	1	↑ 10	[3,17]	0.007
		2	↑ 6	[-9,21]	0.43
		3	0	[-2,2]	0.68

## 13.5 Muscle hypertrophy results

Useable ultrasound data for both the muscle CSA and hyoid displacement measures were obtained for all 20 of the participants in the effortful-swallowing group, but for only 19 of the 21 participants assigned to the modified head-lift group due to problems with data acquisition or data transfer for 2 participants.

### 13.5.1 CSA of submental muscles

Raw data plots for CSA of the left and right anterior belly of digastric muscles and the combined geniohyoid muscles for both the effortful-swallowing and modified head-lift group are presented in Appendix VI.

#### 13.5.1.1 CSA of the left anterior belly of the digastric muscle

Mean CSA for the baseline and outcome sessions are presented in Figure 13.33 for both groups. The standard deviations were .28 cm<sup>2</sup> (32%) across participants and .10 cm<sup>2</sup> (11%) within participants for the effortful-swallowing group, and .19 cm<sup>2</sup> (24%) and .17 cm<sup>2</sup> (22%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.34.

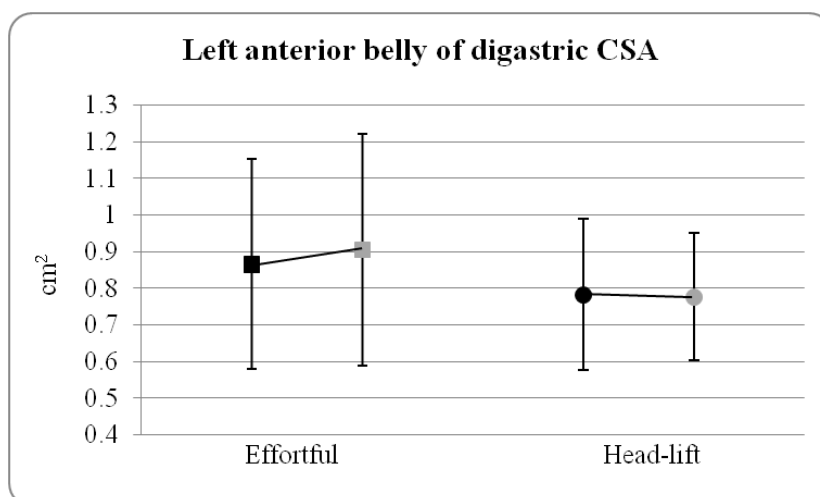


Figure 13.33. Group means and standard deviations of CSA of the left anterior belly of digastric muscle.

**Table 13.34. Estimated effects of six weeks of exercise on the CSA of the left anterior belly of the digastric.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-3%	5%	13%	0.24	-14%	-1%	12%	0.90

### 13.5.1.2 CSA of the right anterior belly of the digastric muscle

Mean CSA for the baseline and outcome sessions are presented in Figure 13.34 for both groups. The standard deviations were .29 cm<sup>2</sup> (32%) across participants and .12 cm<sup>2</sup> (13%) within participants for the effortful-swallowing group, and .15 cm<sup>2</sup> (19%) and .14 cm<sup>2</sup> (17%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and *p*-values are provided Table 13.35.

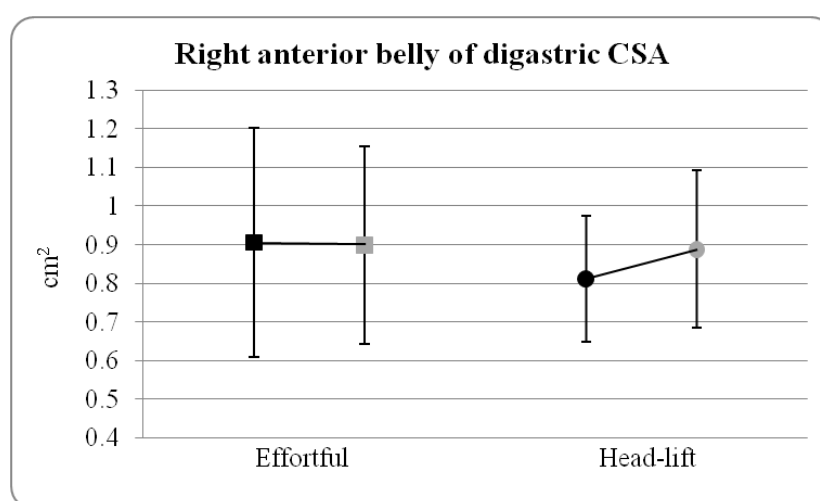


Figure 13.34. Group means and standard deviations of CSA of the right anterior belly of digastric muscle.

Table 13.35. Estimated effects of six weeks of exercise on the CSA of the right anterior belly of the digastric.

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-10%	-1%	8%	0.84	0%	10%	20%	0.06

### 13.5.1.3 CSA of the combined geniohyoid muscles

Mean CSA for the baseline and outcome sessions are presented in Figure 13.35 for both groups. The standard deviations were .71 cm<sup>2</sup> (38%) across participants and .70 cm<sup>2</sup> (37%) within participants for the effortful-swallowing group, and .49 cm<sup>2</sup> (30%) and .47 cm<sup>2</sup> (29%) for the modified head-lift group. There was no evidence of an effect of treatment for the

effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and  $p$ -values are provided Table 13.36.

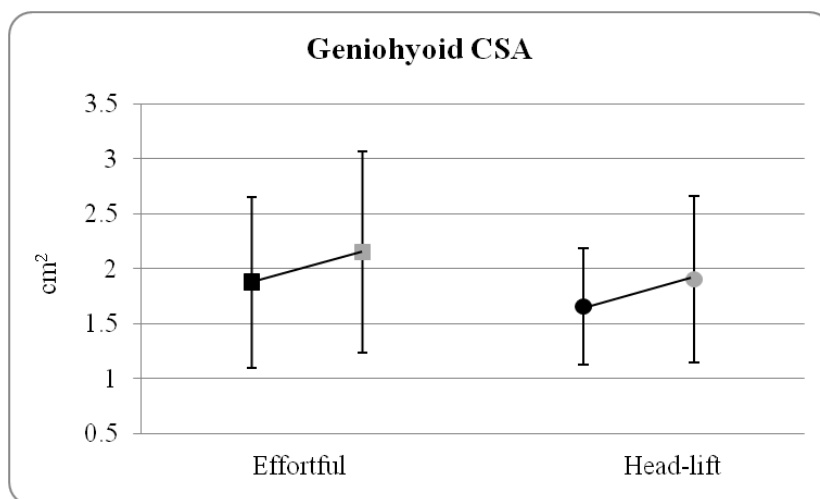


Figure 13.35. Group means and standard deviations of CSA of the combined left and right geniohyoid muscles.

**Table 13.36. Estimated effects of six weeks of exercise on the CSA of the combined left and right geniohyoid.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	$p$	Lower	Estimate	Upper	$p$
-6%	15%	36%	0.16	-1%	15%	31%	0.07

## 13.6 Hyoid displacement results

Raw data for percent change from rest to maximal displacement for both the effortful-swallowing and modified head-lift group are presented in Appendix VI.

Mean percentage change of hyoid from rest to maximal displacement for the baseline and outcome sessions are presented in Figure 13.36 for both groups. The standard deviations were 7% (33%) across participants and 5% (24%) within participants for the effortful-swallowing group, and 9% (43%) and 9% (43%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and  $p$ -values are provided Table 13.37.

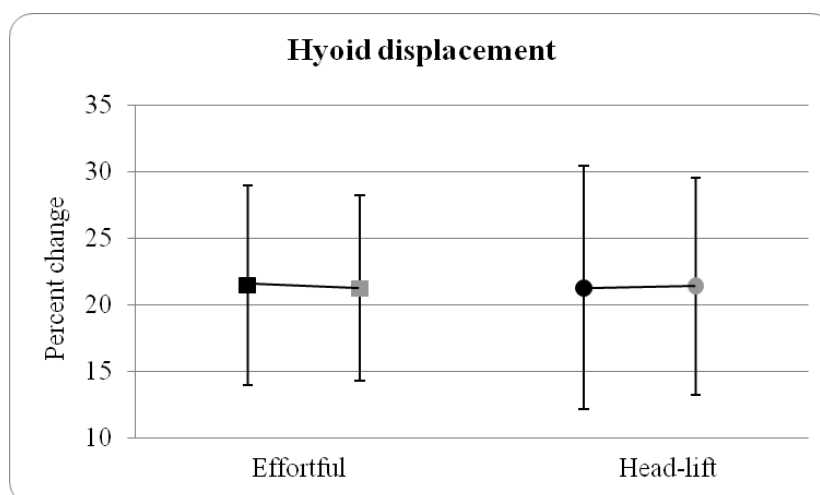


Figure 13.36. Group means and standard deviations of percent change of hyoid displacement from rest.

**Table 13.37. Estimated effects of six weeks of exercise on the percent change of hyoid position from rest to maximal displacement.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-10%	0%	10%	0.84	-20%	0%	20%	0.95

## 13.7 Muscle activation results

As sEMG measures were taken in conjunction with MEP measures, participants who did not have MEPs did not return to the MEP lab for the outcome session. The researcher was therefore not prompted to collect outcome sEMG measures, and only determined this oversight once data collection had been initiated. This, combined with unsatisfactory data, resulted in the smallest number of contributing participants for sEMG measures. Of the 20 assigned to the effortful-swallowing group, 13 had useable data available from both the baseline and outcome session. Of the 21 participants assigned to the modified head-lift group, 18 had useable data available from both sessions. Raw data plots for EMG values for both the effortful-swallowing and modified head-lift group are presented in Appendix VI.

### 13.7.1 sEMG recorded during maximal volitional contraction

Mean amplitudes for the baseline and outcome sessions are presented in Figure 13.37 for both groups. The standard deviations were 449  $\mu$ V (66%) across participants and 312  $\mu$ V (46%)

within participants for the effortful-swallowing group, and 326  $\mu\text{V}$  (47%) and 203  $\mu\text{V}$  (30%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and  $p$ -values are provided Table 13.38.

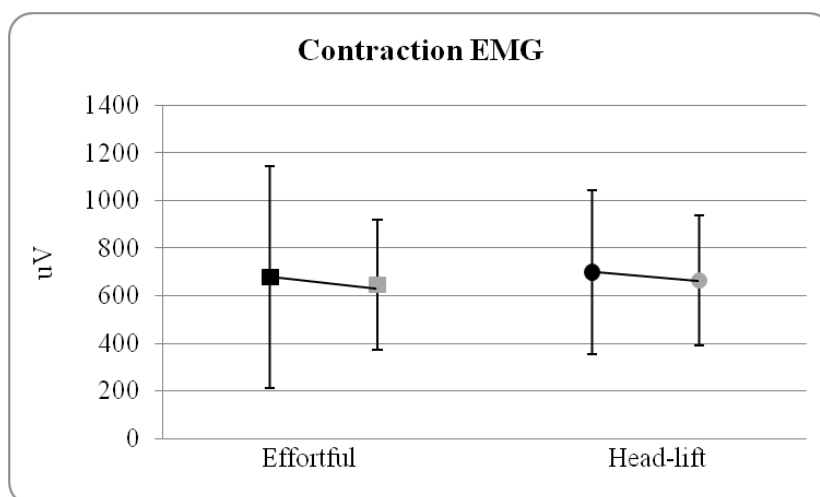


Figure 13.37. Group means and standard deviations of sEMG amplitude during maximal voluntary contraction.

**Table 13.38. Estimated effects of six weeks of exercise on amplitude of EMG recorded during volitional contraction.**

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	$p$	Lower	Estimate	Upper	$p$
-30%	-1%	27%	0.92	-21%	-3%	15%	0.73

### 13.7.2 sEMG recorded during volitional swallowing

Mean amplitudes for the baseline and outcome sessions are presented in Figure 13.38 for both groups. The standard deviations were 165  $\mu\text{V}$  (46%) across participants and 132  $\mu\text{V}$  (37%) within participants for the effortful-swallowing group, and 175  $\mu\text{V}$  (37%) and 130  $\mu\text{V}$  (28%) for the modified head-lift group. There was no evidence of an effect of treatment for the effortful-swallowing or modified head-lift group following six weeks of exercise. The estimated effects, 95% confidence intervals, and  $p$ -values are provided Table 13.39.



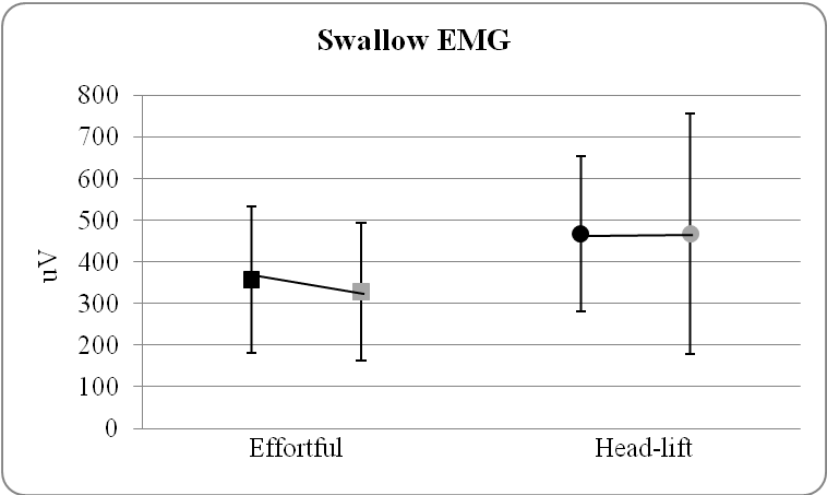


Figure 13.38. Group means and standard deviations of sEMG amplitude during volitional swallowing.

Table 13.39. Estimated effects of six weeks of exercise on amplitude of EMG recorded during volitional swallowing.

Effortful-swallowing group				Modified head-lift group			
Lower	Estimate	Upper	<i>p</i>	Lower	Estimate	Upper	<i>p</i>
-32%	-6%	19%	0.59	-16%	0%	16%	0.97



## Chapter 14: Discussion

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This study assigned 20 participants to an effortful-swallowing treatment paradigm and 21 participants to a modified head-lift manoeuvre to separately assess treatment effects on biomechanical and neural mechanisms of swallowing. This study is the first to document cumulative biomechanical outcomes of an effortful-swallowing exercise protocol. While some investigations have documented cumulative effects of head-lift manoeuvre on swallowing biomechanics, there are discrepancies in the findings. Additionally, no studies have previously investigated changes in corticobulbar excitability associated with the technique. Because of the paucity of literature on the rehabilitative potential of the two techniques, it presents a challenge to prescribe these techniques according to the physiologic needs of the patient. No adaptations in biomechanical or corticomotor functions were revealed following six weeks of either effortful-swallowing or modified head-lift exercise. As each measure warrants various considerations, they will be addressed separately.

### 14.1 Corticobulbar excitability

#### 14.1.1 Cumulative effects of exercise on submental MEPs

Investigation of changes in neural processes is required to provide evidence for the use of rehabilitation techniques to modify swallowing neurophysiology (Martin, 2009; Robbins, et al., 2008). While some studies have documented immediate treatment effects on MEPs, only one study has attempted to address cumulative effects (Gallas, et al., 2009). Additionally, the Gallas study attempted to document changes in excitability of cortical projections during rest, during which the swallowing neural pathways may not be activated. This is the first investigation into cumulative effects (six weeks of treatment) of either an effortful-swallowing or a modified head-lift manoeuvre on MEPs recorded during swallowing.

It was hypothesized that six weeks of effortful-swallowing would facilitate MEPs recorded during both volitional swallowing and volitional contraction of the submental muscles (Hypotheses 1 and 2, Chapter 11). These hypotheses were based on findings that task-oriented skill training influences corticomotor function, measured with MEPs (Koski, et al., 2004; Piron, et al., 2005). The opposite was hypothesized following 6 weeks of modified head-lift manoeuvre (Hypotheses 3 and 4, Chapter 11), predicting no change from baseline in MEPs recorded during both volitional swallowing and volitional contraction of the submental

muscles. This was based on findings that modifications of corticomotor function measured with MEPs are not documented following non-task-oriented strength training (Carroll, et al., 2002; Jensen, et al., 2005).

While research outcomes using the Bonferroni corrected significance value supports the prediction that six-weeks of modified head-lift manoeuvre would not facilitate corticobulbar excitability, the 95% confidence interval around the estimated effect did not include zero. While this indicates there may be a decrease in onset latency of .8 ms (9% from baseline), consideration of the precision estimates provided by the within-participant standard deviation is warranted. The variance associated with repeating the measure was 1.4 ms (16% from baseline), suggesting that the sensitivity of the current study was insufficient to detect such a decrease. The fact that no other MEP measures were modified following the modified head-lift manoeuvre, and because the presence of a real effect being detected with sufficient power would likely result in a much smaller *p*-value, the probability is that this finding did, in fact, represent a Type 1 error. Alternatively, if this effect is real and has been revealed because of sufficient participant numbers, the fact that this change is substantially less than the change resulting from repeating MEP procedures alone suggests it is of little clinical relevance. The lower limit of the 95% confidence interval of the estimated effect suggests the effect could be extremely close to zero, supporting either possibility.

Assuming this position, the prediction that modified head-lift manoeuvre would not facilitate excitability of cortical projections to the submental muscles can be accepted, supporting the findings that strength training without a skill component does not induce higher level adaptations. A specificity of practice phenomenon has been reported for limb muscles following non-task-oriented strength training, with improvements in strength found not to generalize to functional movement outcomes. Therefore, the possibility that swallowing may differ to other neuromuscular tasks in its neural response to strength training was proposed based on the biomechanical adaptations during swallowing documented by some authors (Easterling, 2008; Easterling, et al., 2005; Shaker, et al., 2002; Shaker, et al., 1997). As the present study found no biomechanical changes associated with six weeks of the modified head-lift manoeuvre, these findings support those reported by a recent investigation of the head-lift manoeuvre that also failed to reveal modified biomechanics (Logemann, et al., 2009). The present study is the first to assess cumulative effects of a modified head-lift

manoeuvre on corticomotor function measured with MEPs. The results suggest that a modified protocol of the exercise did not induce changes in the excitability of cortical projections to the submental muscles. This finding is consistent with previous research that found no evidence of neural adaptation following isolated strengthening exercises (Carroll, et al., 2002; Jensen, et al., 2005).

The hypotheses predicting enhanced MEPs following effortful-swallowing are not supported by the current findings. Previous studies have documented increased MEPs during both rest (Koski, et al., 2004) and volitional contraction (Piron, et al., 2005) of the target muscles following functional rehabilitation of patients with limb impairment. The use of healthy participants may have contributed to the lack of significant findings. It is plausible that participants without impaired swallowing function and/or corticomotor function have less scope for adaptation in MEPs. However, the use of healthy participants is a crucial first step for treatment studies. Interpreting patient response is reliant on a prior knowledge of healthy response. If a negative outcome was documented in corticomotor function of healthy participants following effortful-swallowing, it would caution the application of the technique to neurologically impaired patients.

Another possibility is that task-oriented swallowing exercise does not have the same effect on the excitability of cortical projections as task-oriented limb exercise. As the brainstem plays the primary role in execution of the swallowing process, cortical projections may not be reinforced to the same extent during repetitive swallowing as they are during repetitive limb movement. This idea is supported by Doeltgen et al. (2011), who proposed that smaller amplitudes of MEPs measured during volitional swallowing compared with volitional contraction were a result of differential levels of cortical input. One study attempted to document changes in MEPs following one week of effortful-swallowing exercise (Gallas, et al., 2009). While this study reported significant increases following exercise, the methods of MEP acquisition differed from the baseline to the outcome session. Additionally, values obtained from the lead author of this paper (Gallas, et al., 2009) indicated that each raw MEP trial was incorrectly treated as independent in their statistical analysis, thus falsely increasing the significance of any effects; unfortunately this therefore invalidates the findings from their study.

Dose, frequency, and intensity of exercise may also have precluded the effortful-swallowing exercise from influencing corticomotor function. Unlike the head-lift manoeuvre, effortful-swallowing rehabilitation has not previously been assessed according to a specific dose, frequency, and intensity. The current study matched the number of repetitions with that recommended for the head-lift manoeuvre, requiring 33 effortful swallows in one sitting, amounting to 99 repetitions per day, 495 repetitions per week, and a total number of 2970 effortful swallows over the duration of six weeks. If the average amount of exercise reported by participants in the current study is representative of exercise completed, the effortful-swallowing group had an average of 470 repetitions per week (2820 total), with the modified head-lift manoeuvre averaging 468 (2808 total). Increasing the intensity (e.g., having 99 per day done in one session), frequency (e.g., breaking the 99 into five blocks instead of three) or dose (e.g., increasing the total repetitions) may have resulted in significant modification of corticomotor excitability measures. However, increases in muscle morphometry have been documented after eight weeks of exercise involving 270 weekly repetitions of a tongue strengthening exercise (2160 total) (Robbins, et al., 2005; Robbins, et al., 2007). Neurological adaptations are presumed to occur prior to changes in muscle morphometry (Burkhead, et al., 2007), implying that if alterations in MEPs were likely to result from effortful-swallowing, the evaluated protocol would have been sufficient to induce these. Furthermore, the additional benefits of an exercise protocol involving increased dose, frequency, or intensity has to be weighed up against the possible negative effects on exercise maintenance that may result. That is, increasing the requirements of the rehabilitation protocol may result in reduced exercise compliance. As the effectiveness of rehabilitation is largely dependent on exercise attainment and maintenance (Easterling, 2008), increasing the complexity or intensity of the protocol may jeopardize improvements.

Another possible explanation for a lack of alterations in MEPs is actual exercise maintenance versus reported exercise maintenance. Monitoring exercise maintenance during a six-week protocol is problematic. Weekly home visits were conducted in the present study in an attempt to keep motivation levels high and to check the accuracy of exercise execution. Generally speaking, the home visits made it apparent that most participants were familiar with exercise execution. Examples of these situations included some participants predicting the exact duration needed to complete the exercise, some had a specific location set up with a clock positioned so they could monitor the sustained head-lifts, and most showed a progressive ease

of execution suggesting regular practice. However, the possibility remains that exercise maintenance was below that reported. Requiring healthy participants to complete an exercise designed to ameliorate impairments that are not present may decrease motivation.

Another consideration relating to the lack of significant results in MEPs following either exercise is that MEPs were always recorded from actively contracted submental muscles. Andersen (1999) cautions that small fluctuations resulting from intervention may be masked when obtaining MEPs from a contracted muscle. Recording MEPs during active contraction of the submental muscles is necessary for two reasons. Firstly, to test the excitability of cortical projections that are activated with swallowing requires task-specific activation of these projections through swallowing. Changes in cortical projections during rest may not represent changes in neural pathways engaged in swallowing. Additionally, recording MEPs from the submental muscles at rest is problematic and time consuming, with one study documenting recordable MEPs at high stimulus intensities (98%) in only 1 of 15 participants (Doeltgen, et al., 2011). The fluctuations masked by contraction are likely to be relatively small (Andersen, et al., 1999), suggesting the clinical relevance of such fluctuations is questionable.

As no studies have previously documented the cumulative effects (beyond a few hours) of swallowing rehabilitation techniques on MEPs, effect sizes needed to be assumed from studies looking at changes immediately following or during treatment techniques. Therefore, it can be assumed that cumulative effects (if any) in healthy participants were not substantial enough to exceed the reported variance. It is arguable that a treatment effect that is smaller than normal fluctuations has little clinical relevance. Given the large within-participant variance reported in the current data set, it is evident that substantial effects are required to surpass this variance. The issue of large variance is not specific to this study, but rather is inherent to MEP investigations in general, with considerable variance commonly reported. Large standard deviations are typical for effects documented immediately following treatments, ranging from around 50% of the mean (Al-Toubi, et al., 2010; Doeltgen, et al., 2009a) to as high as 140% (Plowman-Prine, et al., 2008). The problem with interpreting this variation is that the relative contributions of trial, session, task, and participant to this total variation are unknown.

To further elucidate the relative contributions of various factors to the substantial variation seen in MEP data, this study reports within-participant variation alongside estimated effects. As suggested by Paine (2006), the size of response variability needs to be taken into account when assessing changes in the excitability of cortical projections. By quantifying this variance, the size of effects required to supersede this can also be obtained. Analysis of the within-participant standard deviations provides an indication of the sensitivity of the MEPs recorded in the present study. Comparisons of the within-participant standard deviations reported in Chapter 7 with those reported for the treatment study suggest that substantial variance is introduced as a result of acquiring repeated measures across different days compared with on the same day, therefore requiring replacement of electrodes, and redefining the optimal site for scalp stimulation. As the variance for each group differed substantially in some cases (see Section 13.3.1.2), this suggests that group values of across- and within-participant variance are sensitive to highly variable individuals. While this variability may reflect true fluctuations in corticomotor excitability, it also reduces the sensitivity of MEP measures to treatment effects. For this reason it is important for studies of corticomotor excitability to assess precision estimates when determining the desired magnitude of change required from a given treatment, or to document change alongside other measures of clinical function. Because group standard deviations reported here are similar to those reported by other investigation of MEPs, this not only strengthens the confidence of the methods used in the current research, but lends to the conclusion that either treatment has no apparent cumulative effect on excitability of corticobulbar projections in healthy participants. Further research is required to document the cumulative effects of the same treatments in patients and to estimate the size of effects that represent clinically significant change in order to assess the sensitivity of MEPs in measuring cumulative treatment effects.

### **14.1.2 Immediate effects of exercise on submental MEPs**

As there are a limited number of studies available with which to compare cumulative results, immediate effects were also recorded. This study found no immediate effects of a single exercise session of either effortful-swallowing or modified head-lift manoeuvre on submental MEPs. As mentioned above, because the head-lift manoeuvre is a strengthening exercise, no effects were expected. While no studies have looked at immediate modifications in corticobulbar excitability following effortful-swallowing, increases were anticipated given the task-oriented nature of the exercise. Because of the difference in exercise duration, and the



comparisons made possible by other studies assessing immediate results, further considerations in addition to those already discussed for the lack of significant findings are warranted.

While cumulative effects may not be evident in healthy participants, immediate effects of treatment on MEPs in unimpaired participants has been documented by numerous studies (Doeltgen, et al., 2010a; Fraser, et al., 2003; Gow, et al., 2004a; Gow, et al., 2004b; Hamdy, et al., 1997; Jefferson, et al., 2009a; Jefferson, et al., 2009b), suggesting a difference in the effects of the exercises used in the present study. Comparison of effect sizes documented by previous studies with the precision estimates of the current study suggests that if effects were of a similar magnitude to those documented previously, they would have been detected here. Increases in MEP amplitudes have been reported of a magnitude of 47% - 150% from pre-treatment values (Fraser, et al., 2003; Gow, et al., 2004a; Gow, et al., 2004b; Hamdy, et al., 1997; Jefferson, et al., 2009a; Jefferson, et al., 2009b), much larger than the within-subject standard deviations reported for immediate MEP effects (24% - 34%). One possibility to explain this difference is that the amount of exercise preceding the assessment of immediate effects in the current study was insufficient to prompt changes in MEPs. One study assessing the immediate effects of water swallowing on pharyngeal and esophageal MEPs found significantly increased amplitude immediately following 120 water swallows (magnitudes ranging from 45% - 76% from baseline depending on the muscle from which MEPs were recorded), but not in recording blocks taken 15, 30, 45 or 60 min after the swallowing task (Fraser, et al., 2003). The current study included approximately one quarter of the repetitions of Fraser's study, with participants completing 33 effortful swallows prior to MEPs being recorded to detect immediate effects. While the decreased number of repetitions may explain the discrepancy, there are additional variables to consider.

The Fraser study utilized water swallowing, thereby incorporating sensory input with the exercise. A large proportion of studies documenting immediate increases in swallowing MEPs utilize sensory techniques such as neuromuscular electrical stimulation (Doeltgen, et al., 2010a; Fraser, et al., 2003; Gow, et al., 2004a), cranial nerve stimulation (Hamdy, et al., 1997), and olfactory and gustatory stimulation (Wahab, et al., 2010). It is possible that cortical excitability may be influenced by sensory treatments to a greater degree than

neuromuscular exercise. While effortful-swallowing incorporates task-oriented proprioception, it is more focused on motor execution than sensory integration.

As discussed in Section 3.1.1.1, MEPs are not a direct measure of any swallowing biomechanical function *per se* but they offer insight into the function of the corticobulbar pathways that may underpin changes in swallowing function. The relationship between changes in MEPs and coincident alterations in swallowing biomechanics is unclear, suggesting further research is required to elucidate the specific functions that may be influenced by changes in corticobulbar excitability. As this study did not reveal changes, either immediate or cumulative, on corticomotor function or biomechanical aspects of swallowing, this issue still remains unclear. If future studies can document changes in the excitability of cortical projections to swallowing muscles alongside simultaneous modifications of biomechanics, insights into the clinical relevance of this neurophysiologic measure can be gained. For example, if increased corticobulbar excitability coincides with improved swallowing function after a given treatment, inferences regarding corticobulbar function as a mechanism behind improved function can be made. Additionally, documenting the size of the effect of treatment on MEP measures that are associated with modification of swallowing function can provide researchers with an idea of the size of clinically significant adaptations in corticomotor function.

## **14.2 Pharyngeal pressures**

Effortful-swallowing is prescribed with an aim of increasing pressure generation for pharyngeal clearance. The head-lift manoeuvre is prescribed to facilitate UES opening. Despite the objectives of the techniques, this study is the first to document cumulative effects of either effortful-swallowing or a modified head-lift manoeuvre on pharyngeal contact pressures. As studies have previously reported increased UES opening following the head-lift manoeuvre measured from VFS (Easterling, et al., 2005; Shaker, et al., 1997), and decreased intrabolus pressures measures with manofluorography (Shaker, et al., 1997), the present study aimed to translate these findings to how the techniques affect functional UES swallowing pressures.

### **14.2.1 Immediate effects of effortful-swallowing on pharyngeal pressures**

The differences in pharyngeal pressures were analysed to determine if, like previous studies, effortful-swallowing increases the magnitude of pharyngeal pressures and UES pressures at the time of execution. These findings revealed that there was an increase in oropharyngeal and hypopharyngeal pressures, and a trend towards increased magnitude of UES pressures for effortful swallows compared with dry swallows. However, the values for the modified head-lift manoeuvre group showed an increase for oropharyngeal pressures only. While this raises concerns regarding the difference between the groups, it suggests that the level of effort recruited by the effortful-swallowing group during the technique was different from regular swallows, therefore demonstrating the potential of the exercise for influencing strength.

### **14.2.2 Cumulative effects of effortful-swallowing on pharyngeal pressures**

#### ***14.2.2.1 Oropharyngeal and hypopharyngeal pressures***

It was hypothesized that oropharyngeal and hypopharyngeal pressures would increase during non-effortful-swallowing following six weeks of repetitive effortful-swallowing (Hypothesis 5, Chapter 11). This was based on the findings that during execution of the technique, oropharyngeal (Lazarus, et al., 2002; Ohmae, et al., 2000; Pouderoux & Kahrilas, 1995) and hypopharyngeal (Huckabee, et al., 2005; Huckabee & Steele, 2006) pressures are facilitated. While some studies have not found any differences in pharyngeal pressures using this technique (Bulow, et al., 1999, 2001), the greater statistical power and repeated findings of studies documenting increases formed the basis of the hypotheses for the present investigation. No cumulative changes were documented in oropharyngeal or hypopharyngeal pressures during dry and 10 mL water swallows following the effortful-swallowing exercise protocol. These results suggest that increases in pressure documented during execution of the technique do not generalize to non-effortful-swallowing in healthy participants. A study assessing changes in lingual pressures associated with age concluded that despite a reduction in pressure reserve with age, pressures during swallowing remain similar across the lifespan (Robbins, et al., 1995). If the same is true for pharyngeal pressures, investigations of healthy adults may show no changes in functional swallowing pressures, regardless of the age of participants. Assessing the cumulative effects of the technique on the pharyngeal pressures of

patients with reduced pharyngeal muscle activation is necessary before drawing conclusions regarding the suitability of the technique in facilitating pharyngeal pressures and clearance.

#### **14.2.2.2 UES pressures**

An increase in the magnitude of UES nadir pressures was predicted to result from six weeks of effortful-swallowing (Hypothesis 6, Chapter 11). This was based on previous studies that have documented increased nadir pressures (Huckabee, et al., 2005; Witte, et al., 2008) and relaxation duration (Hind, et al., 2001; Hiss & Huckabee, 2005; Ohmae, et al., 2000) during execution of the technique. No changes from baseline were found following repetitive effortful-swallowing during dry or effortful-swallowing. While Bonferroni correction suggests the effect of effortful-swallowing on nadir pressure recorded during 10 mL water swallows was not significant at the 0.05 level, 95% confidence intervals did not include zero, warranting consideration of this possible effect. Estimated effects suggest a decrease in the magnitude of negative pressure following the six weeks of exercise. This decrease was sizeable at 50% from baseline. While this raises the possibility that cumulative effects of effortful-swallowing may have created more resistance for transfer of a water bolus into the pharynx, the within-participant precision estimates show that variance across sessions was larger than this estimated effect at 67%. This suggests that if this effect did not result from chance alone, it is of a smaller magnitude than expected from repeating manometry alone, therefore raising questions regarding its clinical relevance. However, as this result was not evident for dry and effortful swallows, it suggests that this finding does not reveal a true effect of the exercise, but is revealed because of chance. As the 95% confidence intervals around this estimated effect are quite large, future studies utilizing more people may assist with narrowing this estimate and obtaining a clearer picture regarding the authenticity of this possible effect. As the presence of a bolus has been shown to influence the magnitude of UES nadir pressures, but not oropharyngeal and hypopharyngeal pressures during effortful-swallowing (Witte, et al., 2008), there is a possibility that the bolus interacts differently with the relatively small lumen of the UES during effortful-swallowing. Further studies investigating the relationship between swallowing biomechanics and a water bolus after effortful-swallowing exercise using manofluorography would help elucidate the mechanisms behind this possible effect.

Specific to dry swallows, repetitive effortful-swallowing does not appear to cumulatively influence UES pressures. Additionally, UES nadir pressures during effortful-swallowing are not enhanced, suggesting that practising the task does not result in progressive changes of the task. These findings have implications for the rehabilitative potential of effortful-swallowing to facilitate pharyngeal clearance and UES opening. The use of healthy participants may explain the lack of change seen following repetitive execution of the technique. An alternate factor to consider is age. In the current study, participants were older adults recruited to represent the age group associated with stroke. It is possible that the cumulative effects are different for this population than for younger participants. While further studies would provide insight into this proposition, the value of documenting change in younger participants as a result of effortful-swallowing, which is typically prescribed for older patients, must be questioned. Further studies need to assess the cumulative effects of the technique on the UES pressures of patients with impaired UES function. This population may provide larger effect sizes that can be detected following six weeks of exercise.

### **14.2.3 Cumulative effects of modified head-lift manoeuvre on pharyngeal pressures**

#### ***14.2.3.1 Oropharyngeal and hypopharyngeal pressures***

It was hypothesized that six weeks of modified head-lift manoeuvre would not influence oropharyngeal or hypopharyngeal pressures during swallowing (Hypothesis 7, Chapter 11). No cumulative effects of head-lift manoeuvre have previously been documented for contact pressures in the pharynx. As head-lift manoeuvre aims to increase activation of the submental muscles for greater traction force on the UES during swallowing, it was not envisaged to impact pharyngeal pressures based on the factors that contribute to pressure accumulation in the pharynx. While no findings reached significance at the 0.05 level according to the Bonferroni corrected  $p$ -value required, the estimated effect of modified head-lift manoeuvre on upper-pharyngeal pressures during effortful-swallowing did not include zero in the confidence interval, deserving consideration. The estimated effect was a decrease in upper-pharyngeal pressures of 13% from baseline. As head-lift manoeuvre aims to increase the submental muscle activation during swallowing, it may be that as increase in anterior pull from these muscle results in reduced strength of the posterior action of the base of tongue towards the posterior pharyngeal wall. As tongue movement contributes to pharyngeal

pressure accumulation (Perlman & Christensen, 1997), it is possible that an indirect effect of the submental muscles influences pressures in the oropharynx. However, the within-participant standard deviation for the modified head-lift group for this measure was 23%, suggesting the sensitivity of the measures here are not sufficient to accurately detect such an effect. Alternatively, if this power revealed a true effect through adequate power, the magnitude of this change is such that it is almost half of the change expected from repeated measures in the absence of treatment. As with the other measures utilized in this study, further research is required to investigate the response of impaired pharyngeal pressures to the head-lift manoeuvre.

### ***14.2.3.2 UES pressures***

An increase in the magnitude of UES nadir pressures was predicted following six weeks of the modified head-lift manoeuvre (Hypothesis 8, Chapter 11). While no studies have documented cumulative effects of the technique on UES pressures, increased maximum anteroposterior opening is reported when measured with VFS (Easterling, et al., 2005; Shaker, et al., 1997). Additionally, the head-lift manoeuvre was devised to create greater traction force on the UES during hyolaryngeal excursion to facilitate UES opening during swallowing. The current study found no differences in UES pressures during any swallow type after modified head-lift exercise. As some studies previously documenting increased anteroposterior opening after the exercise have also found UES adaptations in a control (Logemann, et al., 2009) and sham exercise group (Shaker, et al., 2002), the validity of measures must be questioned. It is also possible that the exercise facilitates increased maximum anteroposterior UES opening, but such adaptations do not affect functional pressures during swallowing. Alternatively, as the nadir of UES relaxation pressure during swallowing reflects the magnitude of hyolaryngeal traction on the UES (Jacob, et al., 1989), it is possible that the increase in UES opening documented by other studies reflects adaptations in factors other than hyolaryngeal traction force. The factors that contribute to UES opening include termination of the neural command inducing tonic contraction of the cricopharyngeus, traction force created by hyolaryngeal excursion, and sphincter distension related to bolus pressure on the UES (Jacob, et al., 1989). Components of UES opening not assessed in the current study, such as intrabolus pressure, may have been modulated by the exercise protocol and gone undetected. Further studies are required to assess the functional repercussions of the previously-documented increase in anteroposterior UES opening. Utilizing VFS in conjunction with

manometry would enhance the knowledge of how the two measures reflect swallowing function.

Alternatively, differences between studies documenting increased UES opening and the current study may explain the discrepancies. As discussed above, the current study utilized healthy participants. Unimpaired UES function may be resistant to change in response to exercise. Two studies documenting increases in UES opening with VFS have utilized patients with dysphagia (Logemann, et al., 2009; Shaker, et al., 2002). However, studies investigating the response of healthy older adults to the technique have also documented similar increases with similar methods (Easterling, et al., 2005; Shaker, et al., 1997), suggesting change was possible in the current study. An alternative explanation is that the slight modification of the technique – reduction of the isometric head-lift from 60 s to 30 s – used in this study diminished the resulting effects on UES pressures. It is important to document changes in UES function in patients for whom this technique is proposed. As it remains unclear how the head-lift manoeuvre influences the biomechanical event it was designed to address, more research is required before the technique can be prescribed with confidence for UES dysfunction.

#### **14.2.4 Factors to consider relating to pharyngeal pressures**

Significant effects of gender and age have been revealed for amplitude and duration of upper-pharyngeal, hypo-pharyngeal and UES pressure generation measured during effortful-swallowing (Macrae et al., 2010). This implies that results of pharyngeal pressure measures made with manometry are influenced by interactions between swallowing conditions and participant demographics. While the current study controlled for gender, it only investigated healthy adults 50 years and over. It is therefore likely that more variation will exist in data sets including younger participants. As age and gender interact with factors such as bolus variables (Butler, et al., 2009), these issues need to be considered when comparing the results of investigations, and when designing studies involving measures of pharyngeal pressures.

Large standard deviations were evident for measures of pharyngeal pressures, ranging approximately 30% - 70% of the mean depending on the sensor and swallow type. Standard deviations of this proportion are commonly reported by studies utilizing manometry (Castell & Castell, 1993; Gumbley, et al., 2008; Olsson, et al., 1996; Olsson, et al., 1995b). This

presents researchers with a challenge in determining treatment effects due to the inherent variability of manometry data. Further research is required to ascertain the size of clinically relevant effects, and to determine if these are comparable between patients and healthy participants. If the intrinsic variability of manometry measures hinders documentation of cumulative change following treatment in patients, its continued use in swallowing research and the treatment of dysphagia needs to be questioned.

### **14.3 Muscle hypertrophy**

Effortful-swallowing and head-lift manoeuvre both incorporate a muscle strengthening component. The effect of these exercises on the morphometry of the swallowing musculature is unknown. Only two studies have investigated hypertrophy of the swallowing muscles (Robbins, et al., 2005; Robbins, et al., 2007), focusing on tongue morphometry. This study is the first to investigate hypertrophy in the submental muscles as a result of neuromuscular exercise.

It was hypothesized that CSA of the anterior belly of digastric muscle and the geniohyoid muscle would increase following six weeks of effortful-swallowing (Hypothesis 9, Chapter 11). This hypothesis was based on findings that greater activation of the submental muscles has been documented during effortful-swallowing (Huckabee, et al., 2005). Similarly, it was hypothesized that submental CSA would also increase following six weeks of modified head-lift manoeuvre (Hypothesis 10, Chapter 11), based on the finding that isometric resistance exercise – a component of the head-lift manoeuvre – of the tongue results in increased volume (Robbins, et al., 2005; Robbins, et al., 2007). However, measures of CSA did not demonstrate any evidential changes from baseline following either exercise.

No studies have previously investigated the effects of repetitive effortful-swallowing on submental muscle morphometry. Although effortful-swallowing recruits increased muscle output compared with non-effortful-swallowing, the resulting level may not be substantial enough to challenge maximal muscle activation. Therefore, despite repetition of swallowing with increased force, the submaximal level of activation during practice may be insufficient to prompt hypertrophic modification of the submental muscles. Alternatively, increased muscle activation in isolation may not be the critical factor in promoting hypertrophy of these



muscles. Increasing resistance or duration of the exercise may better enhance force of these muscles and, therefore, hypertrophy.

Unlike effortful-swallowing, alterations in swallowing muscle morphometry have been confirmed following isometric exercise (Robbins, et al., 2005; Robbins, et al., 2007). The study by Robbins and colleagues documented change in the tongue following lingual exercise rather than exercise of the submental muscles. It is possible that the submental muscles are more resistant to hypertrophy than the tongue, because of their relatively small size and the confined space in which they are located. However, as the isometric portion of the head-lift manoeuvre involves only nine repetitions per day, the substantially lower number of repetitions required of participants in the current study (240) compared with the Robbins' studies (2160) suggests dose issues may contribute to the lack of change. Additionally, the isometric portion of the exercise was modified in this study to 30 s compared with the recommended 60 s recommended by Shaker and colleagues (1997). Future studies assessing the effect of the originally prescribed duration on muscle hypertrophy would determine if this issue influenced the findings here.

Another factor that may have precluded significant changes being documented is the technique used to measure CSA. Ultrasound has been shown to be sensitive to detecting geniohyoid enlargement following radiation therapy (Watkin, et al., 2001). Because of the dissimilar mechanisms underlying hypertrophy following exercise and enlargement following radiation therapy, ultrasound may be more sensitive to the effects of the latter. Additionally, the effects may be larger as a result of radiation therapy, making it easier to detect such changes using ultrasound. The studies by Robbins and colleagues (2005; 2007) utilized MRI to reveal increased tongue volume as a result of hypertrophy; consequently, the sensitivity of ultrasound to such changes remains unknown. Additionally, ultrasound methods specific to this study may have masked effects of muscle hypertrophy. A bite-block was used to ensure participant head position was kept consistent between the baseline and the outcome session. This was considered a necessary precaution to ensure changes in neck flexion did not result in changes in CSA measures due to different muscle length between recording sessions. It is likely that maintenance of the bite-block involved some level of submental muscle contraction and, therefore, true CSA values at rest may have been subjected to enlargement from contraction. This assumption is based on findings that the presence of a bite-block increases

submental muscle activation during swallowing (Spiro, et al., 1994). While the Spiro study did not assess changes in resting EMG during the presence of the bite-block, the increase measured during swallowing may reflect overall adaptations associated with maintaining the bite-block. An amplified level of contraction may mask any changes in the muscle morphometry at rest. However, as the bite-block was utilized for both sessions, the level of contraction was presumably similar for the two recordings. However, the within-participant precision estimates suggests that there was substantial differences in the variance across groups and muscles (ranging from 11% - 37%), suggesting the bite-block may have contributed to this variance. Further research is required to assess the effects of the bite-block on the CSA of the submental muscles at rest, and to compare the variance, and therefore precision of the measure when stringent controls are not utilized. Additionally, deducing whether hypertrophy is reflected in these muscles during rest, contraction, or both will provide direction for further studies attempting to document submental CSA with ultrasound.

Another consideration is the likelihood that healthy muscles undergo hypertrophy. It may be that without disease affecting the muscle or innervation of the muscle, adaptations to morphometry are less likely than in patients who show signs of atrophy. The participants in this study were aged 50 years and above to target the age group in which stroke is likely to occur. A study by Robbins and colleagues (1995) proposed, among other possibilities, decreased muscle mass associated with age as an explanation for decreased swallowing pressures in their cohort of healthy participants with a mean age of 75 years compared with their younger counterparts. Additionally, another study by Robbins found increased tongue muscle volume in healthy participants aged 70 years and above following isometric exercise (Robbins, et al., 2005). As age-related changes in muscle structure are relatively small until after the age of 70 (Carmeli & Reznick, 1994), the mean age of participants in the current study (69 years) may have decreased the likelihood of submental muscle adaptations. Further studies are required to assess submental muscle modifications in patients with atrophy and in healthy participants aged over 70 years to document whether hypertrophy of these muscles is possible.

## **14.4 Hyoid displacement**

As hyoid displacement is a crucial component of airway protection and UES opening during swallowing, it is a common target of many rehabilitation techniques. The effect of effortful-

swallowing and head-lift manoeuvre on this biomechanical event is not clear. There is some evidence that negative consequences may result from effortful-swallowing but the cumulative result has not previously been documented. This study is the first to investigate cumulative effects of effortful-swallowing exercise on hyoid displacement. As previous research has found conflicting results regarding the effect of the head-lift manoeuvre on the various components of hyolaryngeal excursion, this study sought to clarify these discrepancies.

It was hypothesized that the degree of hyoid displacement would not differ from baseline following six weeks of effortful-swallowing (Hypothesis 11, Chapter 11). This lack of change was predicted based on results that have demonstrated that extent of hyoid displacement is reduced (Hind, et al., 2001) or unchanged during the technique (Wheeler-Hegland, et al., 2008) compared with non-effortful-swallowing. It was also hypothesized that no change would be documented in hyoid displacement following the six weeks of the modified head-lift manoeuvre (Hypotheses 12, Chapter 11), based on studies that have failed to reveal changes in anterior displacement of the hyoid following six weeks of the technique (Logemann, et al., 2009; Shaker, et al., 2002; Shaker, et al., 1997). Despite being expected, this decrease seems paradoxical with the presumed increase of submental muscle strength proposed to result from the technique. There was no evidence of adaptations to hyoid displacement following either exercise in the current study.

A lack of effect following effortful-swallowing exercise may be a result of co-activation of antagonist muscles working against anterior hyoid displacement. As the technique encourages maximal effort from all oral and pharyngeal muscles with the command “swallow hard” (Hind, et al., 2001), muscles other than the submental muscles, such as the pharyngeal constrictors, are likely to demonstrate a similar increase in activation. It is possible that repetitive effortful-swallowing increases strength in all oral and pharyngeal muscles, thereby negating any effects of increased submental muscle strength.

Alternatively, as swallowing is executed at a submaximal level of isometric muscle strength (Robbins, et al., 1995), it is possible that despite increasing muscle activation at the time of execution, like non-effortful swallows, effortful-swallowing also fails to challenge maximal activation levels. Therefore the repetition of a submaximal level of activation may be insufficient to cause cumulative changes in submental traction force on the hyoid during

swallowing. Another explanation may be the dose, frequency and/or intensity of the effortful-swallowing protocol as discussed above. Increasing the intensity of the exercise may assist with inducing fatigue in the muscles and facilitate practice at maximal levels of activation as a result. This option would need to be investigated to confirm its effects, and also raises the issue of exercise maintenance if lengthy fatigue-inducing sessions are required.

Another possible reason for a lack of change in hyoid displacement following effortful-swallowing is the use of healthy participants. The study reporting unchanged displacement during execution of the technique (Wheeler-Hegland, et al., 2008) also investigated healthy participants. One limitation with this interpretation is that reduced hyoid displacement has also been documented in healthy participants during execution of effortful-swallowing (Hind, et al., 2001), implying that not only is change possible in these participants, but that the ensuing result may be negative. This study did not reveal evidence of negative cumulative effects on hyoid displacement, suggesting despite the possibility of reduced displacement during execution of the technique, this does not translate to cumulative effects during non-effortful-swallowing in healthy participants.

The findings that anterior laryngeal excursion (Easterling, et al., 2005; Shaker, et al., 2002; Shaker, et al., 1997), but not anterior hyoid excursion (Logemann, et al., 2009; Shaker, et al., 2002; Shaker, et al., 1997), is facilitated by six weeks of head-lift manoeuvre, suggest the dose, frequency and intensity of the exercise is sufficient to prompt changes in swallowing biomechanics. Despite the slight modification of the exercise protocol in the current study, the results fit with the previous findings regarding the cumulative effects of head-lift on hyoid displacement. The infrahyoid muscle activation documented during the head-lift manoeuvre (Alfonso, et al., 1998; Ferdjallah, et al., 2000; Jurell, et al., 1997; Mepani, et al., 2009; White, et al., 2008) raises the possibility that any increase in traction force resulting from increased submental muscle activation may be negated by a similar increase in strength of the infrahyoid muscles. As more of the infrahyoid muscles activated during the head-lift manoeuvre have connections with the hyoid than the thyroid cartilage, this may explain the discrepancy in displacement changes of these two structures. The effects of this discrepancy on UES opening and airway protection require further investigation. As the results of the present study failed to reveal changes in UES relaxation pressures following modified head-lift exercise, the balance of increased submental and infrahyoid strength may not be sufficient

to aid UES pressures. This assumption could only be clarified with further investigation that includes measures of laryngeal displacement, hyoid displacement, submental and infrahyoid activation, as well as UES function.

While the results documented in this study are in agreement with those previously reported for head-lift manoeuvre, and fit with what might be expected from effortful-swallowing rehabilitation given the lack of change in hyoid displacement during execution of the technique, identifying limitations of the current methods is warranted. As mentioned in the discussion on hypertrophy of the submental muscles, it has been shown that a bite-block influences the activation of the submental muscles during swallowing (Spiro, et al., 1994). Increased activation of the submental muscles prior to swallowing may decrease the measured resting distance between the hyoid and the mentalis of the mandible. While bite-block positioning was consistent across recording sessions, reducing the distance travelled by the hyoid by inducing muscle activation with the bite-block may have masked any effects of increased displacement. This is supported by another ultrasound investigation that reported reduced hyoid displacement in sequential swallows compared with discrete swallows (Chi-Fishman & Sonies, 2002b). The authors proposed that sustained muscle activity throughout the series of swallows may be the basis for decreased displacement. Alternatively, maintaining the bite-block in the mouth prior to measurement acquisition may fatigue the muscles, altering the activation levels during swallowing. Due to the use of a reference point by which to quantify hyoid displacement, it was considered essential to control participant positioning across the two recording sessions. Differences in neck flexion would alter the measures of the resting distance between the mentalis of the mandible and the hyoid. Further research is required to investigate the influence of the positioning controls used in the current study on true values of hyoid displacement. The standard deviations in hyoid displacement show that within-participant variance for percent change of maximal hyoid displacement from rest varied across the groups, ranging from 24% - 43% from baseline values. This suggests that some people were more variable than others, and therefore influenced group values. Therefore, further investigation is required to assess if the positioning controls increase the variance, therefore decreasing the sensitivity to change, as well as assessing if they introduce limitations in measuring true values of displacement.

The methods of measuring hyoid displacement used in this study did not distinguish between anterior and superior hyoid movement. As mentioned by Stone (2005), distinguishing between true anterior displacement and superior-anterior displacement is not possible from ultrasound. The distances measured reflect the positioning of the transducer. Consequently, more reference landmarks are required to determine true superior and anterior displacement values. While a difference can be seen between superior motion and anterior motion using ultrasound, the two often occur together. Additionally, many participants differ in the timing of superior and anterior motion during swallowing. For example, while all participants had displacement in both directions occurring together, some participants had obvious superior movement at the initiation of hyolaryngeal excursion, while others demonstrated superior motion immediately prior to maximal displacement measures. This is supported by research demonstrating large variation in activation patterns and temporal relationships between the submental muscles (Spiro, et al., 1994). Therefore, measures were taken at the brief pause in hyolaryngeal excursion representing maximal displacement (Chi-Fishman & Sonies, 2002b). In some cases, this involved including a superior movement at the termination of anterior movement that increased the distance between the two reference points. While it is possible that measuring only anterior displacement may have produced different results, the method of measuring each excursion at the point of maximal anterior-superior displacement was necessary to alleviate discrepancies in measurement criteria across participants.

## **14.5 Muscle activation**

Effortful-swallowing and head-lift manoeuvre are designed to facilitate muscle activation during swallowing but no studies have documented the cumulative result of either of these techniques on muscle output during swallowing. This information is necessary to provide evidence of the desired outcomes. This study is the first study to document cumulative effects of either technique on submental muscle activation during swallowing and maximal voluntary contraction.

It was hypothesized that six weeks of effortful-swallowing would improve submental sEMG amplitudes during volitional swallowing and maximal voluntary contraction (Hypotheses 13 and 14, Chapter 11). It was hypothesized that sEMG during maximal voluntary contraction but not volitional swallowing would increase following six weeks of modified head-lift manoeuvre (Hypotheses 15 and 16, Chapter 11). These hypotheses were formulated based on

the findings that a specificity of training (Rose & Christina, 2006) is seen for improvements of strength, with increased activation not generalizing to untrained tasks (Liu-Ambrose, et al., 2003; Rasch & Morehouse, 1957). As effortful-swallowing is a task-oriented strengthening exercise, it was hypothesized that its influence on muscle activation would extend to the functional task of swallowing. As maximal voluntary contraction is measured with isometric contractions, the head-lift manoeuvre would presumably increase isometric activation following six weeks of repetition. No differences were documented in volitional swallowing or volitional contraction sEMG following modified head-lift manoeuvre or effortful-swallowing.

There are a few possibilities that could explain a lack of enhanced sEMG measures following effortful-swallowing. While increased sEMG may occur at the time of execution, the cumulative effect of this increase may not transfer to non-effortful-swallowing. As suggested by Robbins and colleagues (2005), muscle strength may increase following strengthening exercise, however, regular non-effortful swallows may not engage this additional activation. One problem with this interpretation is that maximal voluntary contraction was also unaffected by repetitive effortful-swallowing, raising speculation that maximal strength of the submental muscles was not facilitated. It is possible that effortful-swallowing did not increase activation of the submental muscles to a level necessary to induce cumulative changes. Alternatively, a lack of increase in maximal voluntary contraction may be a result of a specificity of practice whereby strength gains are not transferred to isometric contractions. One way of testing this theory would have been to assess sEMG amplitude during effortful-swallowing prior to and following the six weeks of repetitive effortful-swallowing. This should be considered for future studies to determine if effortful-swallowing impacts any aspect of submental muscle activation in a cumulative sense, and to also determine the importance of muscle strength in non-effortful-swallowing.

While the lack of effect of modified head-lift manoeuvre on sEMG amplitude during swallowing was expected, a lack of change during isometric contraction was not. As mentioned in the discussion regarding muscle hypertrophy (Section 14.3), the isometric portion of the head-lift manoeuvre provides only nine repetitions per day. Additionally, this study utilized a modified duration of 30 s for the isometric contraction. It is possible that this was insufficient to induce changes in the maximal voluntary activation levels of the submental

muscles. As no studies have previously documented cumulative changes in submental muscle activation following six weeks of head-lift manoeuvre, studies need to examine the effects of the originally proposed dose of 60 s. This is essential to assess if the lack of results found in this study are a result of adapted dose or whether they reflect the lack of influence the head-lift manoeuvre has on maximal output of the submental muscles.

An alternative consideration for the lack of changes documented with sEMG is the method itself. As discussed in Section 3.5.1.3, a complex relationship exists between sEMG measures and muscle force (Cooper & Perlman, 1997). Therefore, inferring that a lack of change in sEMG measures is representative of a lack of change in muscle strength may be overlooking the indirect relationship between the two. Factors such as temperature (Myers & Lovelace, 1994) and fatigue (Dideriksen, et al., 2010; Lind & Petrofsky, 1979; Myers & Lovelace, 1994; Shinohara & Sogaard, 2006) have a substantial influence on sEMG amplitudes. As no controls for body temperature or muscle fatigue were utilized in the current study, the lack of changes needs to be interpreted with caution. Additionally, as suggested by some investigators utilizing EMG (Ottenhoff, et al., 1996; Shinohara & Sogaard, 2006), use of a more complex analysis method including temporal and amplitude measures together may provide a more accurate reflection of muscle force. As a linear relationship exists between muscle force and EMG for isometric contractions only, it is likely that measures obtained during swallowing were prone to variation as a result of changing muscle length. The finding that EMG characteristics from the muscles involved in jaw closure are only moderately correlated with force measures (Ottenhoff, et al., 1996), signifies that the linear relationship is likely to be disrupted during swallowing also. Furthermore, while isometric contractions were assessed in the present study, no control over neck flexion was employed across sessions. As muscle length also influences the ability of a muscle to generate force (Lindauer, et al., 1993), variance in neck flexion from the baseline to the outcome session may contribute to a lack of significant changes.

As mentioned in Section 3.5.2, no studies have previously documented within- and across-participant random variation in submental sEMG measures obtained over separate sessions. The precision estimates show that within-participant variation is between 30% - 45% of the mean, suggesting relatively large effect sizes are required to reveal treatment effects. The issues discussed above regarding influences on sEMG amplitudes are likely contributors to



this substantial variation. Any effects of the two exercises examined here can be assumed to be either non-existent, or smaller than this documented variance. Further studies are required to assess the relationship between submental sEMG and mechanical output of these muscles during different tasks as well as the ensuing biomechanical events reliant on submental muscle activation before conclusions can be made regarding the usefulness of sEMG for documenting changes as a result of swallowing treatments.

## **14.6 Limitations**

The limitations of this study need to be emphasized in order to aid the development of future studies looking to document the effects of rehabilitation techniques on swallowing physiology and functional outcomes. This study included a relatively small N for each treatment group. As discussed by Robey and colleagues (1998), phase I research often involves small group observations when exploring the effects of a treatment. As the measures used by this study have not previously been used to document cumulative changes related to either treatment, the effects were unknown, and therefore warranted exploratory investigation (Wheeler-Hegland et al., 2009a). Estimated effects and their 95% confidence intervals are therefore used as primary indicators for treatment effects (as recommended by Beeson & Robey, 2006) and provide evidence beyond the dichotomy of significant versus non-significant findings. While these confidence intervals give the range in which real treatment effects are likely to be situated, a larger participant sample would assist with narrowing the confidence intervals around these estimated effects. Many of the estimated effect intervals are smaller than the within-participant variation, suggesting that reducing the range of the confidence interval would still reveal estimated effects that are smaller than the inherent variance of repeating the measure. However, in some instances the intervals of the estimated effects exceeded the within-participant variance, indicating a reduction of the intervals may reveal treatment effects.

The use of novel measures, or adaptations to measures used previously, could also be viewed as a limitation of this research. This was done in an attempt to expand the resources and measures available to the swallowing researcher and in an attempt to minimize the variability inherent in many measures (e.g., using a reference point for measuring hyoid displacement with ultrasonography). An ultimate approach would have been to incorporate previously used measures alongside the novel and adapted measures in this study. VFS is the measure used

frequently in documenting the changes associated with repetitive head-lift exercise (Easterling, et al., 2005; Logemann, et al., 2009; Shaker, et al., 2002; Shaker, et al., 1997). As mentioned in Section 3.4.1, there is difficulty in obtaining approval from ethical review boards for exposing healthy participants to ionizing radiation in the absence of direct participant benefit. Additionally, the cost of incorporating VFS as an additional measure is substantial, with this study requiring 82 VFS sessions to allow pre- and post-exercise comparisons within each treatment. As mentioned in the discussion of the various measures used in this study, future research aiming to compare results of those which have demonstrated sensitivity to cumulative treatment effects will further the validation of novel measures and expand the toolbox for the swallowing researcher.

As acknowledged throughout this discussion, this study utilized healthy participants. This approach is considered a necessary first step in a meticulous approach to validation of dysphagia management techniques (Logemann, 2005). However, the use of only healthy participants raises the possibility that a lack of significant results will represent a lack of impairment and scope for change in the participant sample. Without the restrictions on time and cost inherent in doctoral research, an ideal progression would be to extend assessment of the effects of either treatment on dysphagic patients. This issue highlights the many components nested within the many phases aimed at providing evidence of efficacy and effectiveness of any treatment (Robey & Schultz, 1998; Robey, 2004; Rosenbek, 1995). This study offers a contribution to the phase I evidence for both effortful swallowing rehabilitation, and a modified head-lift protocol. The research has provided a basis for numerous further studies to address effects of these treatments and the measures used to document such effects.

Another issue that limits the interpretation of the findings presented in this research is regarding dose, frequency, and intensity of treatment. This issue is not specific to this study, but rather reflects the paucity of empirical evidence regarding the optimal characteristics for exercise protocols aiming to induce long-term physiologic and functional change in swallowing. No accepted protocol exists for the use of effortful-swallowing rehabilitation. The number of repetitions was guided by the only widely accepted protocol available for swallowing rehabilitation exercise, offered by the head-lift manoeuvre literature. This does not preclude the scenario that dose, frequency, and intensity of either treatment were not sufficient to induce detectable change in the measures used. Research into the physiologic

adaptations of muscular effort associated with the commonly prescribed head-lift protocol suggests that greater change may be achieved following practice extending over the recommended 6-week period (White, et al., 2008). Investigations such as that completed by White and colleagues are crucial for progression of rehabilitation research through to the later phases of documenting efficacy and effectiveness (Robey & Schultz, 1998; Robey, 2004).

There is a limitation to the treatment study design that needs to be highlighted. This study was exploratory in the sense that no previous studies have document the effects (across time) of either of these two treatment techniques on the biomechanical aspects and corticomotor function investigated in this research. As such, the study was designed as an exploratory, phase-I study (Frymark et al., 2009; Robey & Schultz, 1998; Robey, 2004) to collect preliminary evidence on the effects of these two exercises on the measures utilized. Robey and colleagues (1998) suggest that enrolling participants in a control group for phase-I research may be premature. Having some estimate of the size of possible effects is a suitable first step before increasing the number of participants and cost of research through controlled comparisons. An evidence-based systematic review of oropharyngeal dysphagia behavioural treatments found 17 studies investigating the effects of manoeuvres on healthy participants (Frymark, et al., 2009). Of the 17 studies identified, all of them utilized a similar design to that employed by the current study, in that they did not include a control group (see Wheeler-Hegland et al., 2009a for a review). While all of these studies were examining the immediate effects of interventions on swallowing physiology, a study of healthy participants documenting cumulative changes following the head-lift manoeuvre also utilized the same study design with no control group (Easterling, 2005). Frymark (2009) describe this study design as exploratory, and deem it appropriate for the investigation of healthy participants, and for exploring the physiologic variables that are potentially affected by the target treatment(s). While the lack of significant effects was not anticipated during the design of this study, the results of the present study support the notion that some evidence of effects is desirable before requiring additional input from participants to control against an absence of effects (Frymark, et al., 2009; Robey & Schultz, 1998; Robey, 2004; Wheeler-Hegland, et al., 2009a). As the participants recruited in this study were healthy, it is unlikely that they would show any change between baseline and six weeks post-therapy, given there is no obviously plausible mechanism by which healthy participants would show spontaneous change in the

measures utilized in this study (through mechanisms such as fatigue or learning). It was important to demonstrate whether or not either of these treatments could induce change in healthy individuals before exploring the treatment effect of either paradigm in patient populations. Because there are many possible mechanisms by which change may be seen in the absence of treatment in patient cohorts, such a study would require the use of a control group. However, many phase I studies of disordered participants also omit the use of control groups (Crary, et al., 2004; Drake, O'Donoghue, Bartram, Lindsay, & Greenwood, 1997; Farooqi-Shah & Graham, 2011; Katz & Carlisle, 2009; Lagorio, Carnaby-Mann, & Crary, 2010; Nagaya, Kachi, Yamada, & Sumi, 2004; Regan, Walshe, & Tobin, 2010; Shanahan, Logemann, Rademaker, Pauloski, & Kahrilas, 1993), with this design considered acceptable for exploratory investigations (Ashford et al., 2009; Robey & Schultz, 1998; Robey, 2004). Caution was exercised in all measures to minimize the possibility of documenting any changes related to methodological error. These points notwithstanding, this explanation is not intended to debate the importance of control groups. A control group is crucial in clinical populations to provide evidence that any treatment effects are in fact related to the treatment, and do not represent spontaneous recovery. It could be argued that if any treatment effects had been documented in this study, they would need to be interpreted with caution based on the fact that no control group was utilized, requiring further investigation in a controlled study design to provide phase II evidence. The value of control groups cannot be underestimated and further work in this area should include control groups.

## **14.7 Summary**

In summary, this study revealed no adaptations of biomechanics or corticobulbar excitability following six weeks of either effortful-swallowing or the modified head-lift manoeuvre. Three explanations can be proposed to explain the absence of significant effects. Firstly, the use of healthy participants may have precluded improvements in swallowing function. Secondly, there may have been effects of treatment, but not in the measures utilized. Thirdly, there may have been effects of exercise but these were not of sufficient magnitude to be revealed using the measures and with the number of participants utilized in the current study. While it is likely that effects smaller than the variance could occur given the sizeable variance documented for many of the measures, treatment effects that are substantially smaller than the change that occurs from simply repeating a measure are presumably of little clinical relevance. A combination of all three factors is also possible.

Further investigation is required to assess the response of patient populations to the techniques. Patients may demonstrate greater change in biomechanical aspects and corticomotor function associated with swallowing in response to these exercises. As immediate effects of effortful-swallowing have been reported for healthy participants, it is possible that the cumulative response of non-effortful-swallowing does not mimic those documented during execution of the technique. However, the fact that cumulative effects of the head-lift manoeuvre have been reported in healthy participants suggests that the measures used in the current study did not reflect changes reported by others. In addition to utilizing patient participants, additional measures may elucidate changes that were not evident in the current study. For example, findings from previous studies of an increase in maximum anteroposterior UES opening revealed using VFS (Easterling, et al., 2005; Shaker, et al., 1997), and a decrease in intrabolus pressure shown using manofluorography (Shaker, et al., 1997) after the head-lift manoeuvre may not translate to swallowing pressures measured with manometry in the current study.

If effects documented during execution of manoeuvres are not reinforced as cumulative adaptations in non-manoevr swallows, the choice of measures is a crucial consideration for research into swallowing rehabilitation. Many of the measures showed large within-participant variation, suggesting the magnitude of cumulative effects required from treatments need to also be substantial. Despite their frequent use in swallowing research, very few studies have compared within-participant variation with effect sizes obtained with these measures. Large participant samples would make it possible to reveal small effects, but the comparison of these effects with precision estimates provides some insight into their functional significance. For example, an effect that is substantially smaller than the change revealed from simply repeating the measure may have minimal functional impact. Immediate effects of various treatments have been documented utilizing many of the measures utilized in this research, with the magnitude of these effects exceeding the variance reported here. Research is now required to confirm the magnitude of cumulative effects, which need to be of a similar size or larger than immediate effects to prove efficacious utilizing these measures. As no such effects were documented here, it can be concluded that six weeks of effortful-swallowing or a modified head-lift exercise protocol resulted in no such changes in the measures specific to this study for a healthy-older population. The possibility of increased variance in patient populations implies that treatment effects in such groups would need to be

similarly heightened to be revealed by these methods. While comparison of effect sizes with precision estimates provides insight into whether an effect is smaller, comparable to, or larger than the change documented in the absence of treatment, this may still underestimate the magnitude of a clinically significant response. Therefore, clinically relevant effect sizes need to be determined in patient populations to allow researchers to accurately predict sample size and appropriate measures. By continuing to utilize such measures without knowledge of their precision or the magnitude of effects considered clinically relevant, the risk of dismissing efficacious treatments or developing ineffectual techniques threatens dysphagia management.

Another area for future research is documenting how changes in these measures are accompanied by simultaneous changes in other swallowing functions. This knowledge will enhance the functional application of these measurement tools. For example, many factors influence cortical excitability, and very few studies have investigated how changes in MEPs occur in conjunction with changes in swallowing function. The clinical relevance of modifications in MEPs and other measures such as sEMG may be enhanced by gaining insight into how these changes can promote or enhance swallowing function. It is known that plasticity of corticomotor structures is associated with recovery after injury, and documenting change in both corticomotor and swallowing function may assist with our understanding of the role of such plasticity in recovery of dysphagia.

If patient research demonstrates similar results to the present study, the rehabilitative application of these treatments needs to be queried. Prior to this conclusion, thorough investigation of all possible relevant biomechanic and neurophysiologic adaptations must occur in appropriate patient populations. Additionally, the size of clinically relevant effects must be determined to ensure researchers can accurately power their studies to detect such effects, especially in the face of large variance. This research represents a contribution towards the much needed evidence base for swallowing rehabilitation techniques currently used in dysphagia management. As it addresses the response of a select number of measures to two exercise techniques for a healthy older-age population, there is still a substantial amount of research to be completed for definitive conclusions to be reached.

In summary, there is much research required to confirm the effects of these exercises on swallowing biomechanics and corticobulbar excitability for relevant populations. Prior to this

being achieved, application and interpretation of measures used in swallowing research need refinement. Defining the functional relevance of changes in measures that do not directly assess a swallowing function will allow greater insight into how modulation of the two functions may occur together. Further studies need to provide measures of variance and estimates of clinically significant effects to enable effective evaluation of dysphagia treatments. The substantial variation documented for healthy participants in the current study highlights the increasing need for such assessments. While the expansion of swallowing rehabilitation research is encouraging, the fundamental aspects of this research need to be improved in order to enhance the confidence in the findings from these studies. Clinical management of swallowing disorders must be directed by empirical evidence; therefore this vital information is a prerequisite to the elimination of the burden of dysphagia.





## **PART IV: CONCLUSION**



## Chapter 15: Conclusion and future research

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The results from the methodological studies and the treatment study combined raise concerns regarding the interpretation of measures used in swallowing research. A major restriction is the caused by limited knowledge of what constitutes functionally relevant effects. Because the precision of many measures is unknown, designing studies to assess the cumulative effects of treatment is difficult. Further complicating this process is a lack of data reporting the magnitude of cumulative response to treatment. More research is required to document the long-term effect of treatments on pertinent populations. As any magnitude of change can be revealed with sufficient participant samples, and also not revealed with insufficient participant samples, the distinction between statistically significant effects and clinically relevant effects requires investigation. The variance documented throughout the studies in this thesis provide one step in this process by providing precision estimates, or indicating the sensitivity of the measures used. This research also aimed to document adaptations in biomechanical swallowing events alongside indirect measures such as MEPs, sEMG, and pharyngeal manometry in an attempt to reveal effects that have some clinical relevance to swallowing function. It is therefore unfortunate that no modifications were documented following either exercise in the treatment study. However, as healthy participants are not the target population for the head-lift manoeuvre or effortful-swallowing techniques, the precision and responsiveness of these measures are now required for patient populations to determine their application in dysphagia research and clinical evaluation.

While considerable research is required to improve the methods and evidence for the treatments used in dysphagia management, this issue is not specific to the investigation of swallowing. Thorough explication of reliability, precision, validity, and responsiveness of swallowing measures is an immense undertaking, limited by the vast array of patient populations and the many contexts in which assessment occurs. Researchers must continue to be mindful of the need for robust measures to provide the vital empirical evidence needed for enhanced clinical management of dysphagia. Each measure has relative strengths for investigating specific aspects of swallowing, such as, FEES for airway protection and manometry for pharyngeal pressures. Therefore, a practical approach to enhancing swallowing research would be to develop specific measures as a gold-standard for specific swallowing functions.

The results of Part III show no adaptations in swallowing biomechanics or corticobulbar excitability following six weeks of effortful-swallowing or modified head-lift manoeuvre. While the findings indicate that these neuromuscular exercises have no cumulative effects on the specific biomechanical and neurophysiologic measures assessed in this study, other possibilities must be considered for a lack of observed change. These exercises are designed for the rehabilitation of dysphagic patients in which swallowing function is impaired. The investigation of healthy participants is considered a necessary first step in a meticulous approach to validation of dysphagia management techniques (Logemann, 2005). However, the use of healthy participants in the current research may have resulted in a ceiling effect, therefore failing to induce any improvements in swallowing function. Another important consideration is the capacity to reveal small treatment effects using measures that are highly variable. The number of participants utilized in the current study combined with the possibility that effects were slight implies that the limitations of the measures may have precluded the exposure of such effects. A caveat on this consideration is the clinical significance of change resulting from treatment that is of smaller magnitude than that arising from repeating the assessment in the absence of treatment. Therefore, while small effects may be revealed with larger participant samples, it appears the relevance of these possible effects is minimal under the specific conditions investigated by the current research. As mentioned above, effects may be larger in patient populations, however, precision estimates are also required of such populations to ensure the sensitivity of measures is adequate to treatment effects.

## **15.1 Future research**

Chapter 5 provides evidence of high intra- and inter-rater agreement for data analysis of hyoid displacement utilizing an anatomical reference point with ultrasound images. The results suggest that future studies using ultrasound can avoid complex data calibration and transformation with use of the mentalis of the mandible as a reference point for the hyoid. Therefore, opportunity for clinical application of ultrasound in documenting hyoid displacement and more frequent repetition of non-invasive assessment is increased. While hyoid data analysis from ultrasound appears highly reliable, further research is required to assess the reliability and precision of data acquisition. If repeated-measures are required, the methods used in Chapter 5 may not provide adequate control of methodological variance, such as head and transducer positioning. The methods utilized in the treatment study took

measures to minimize variance due to changes in positioning. However, the effect of the bite-block on hyoid displacement is not clear. Therefore, future investigations need to elucidate the need for stringent position controls by documenting the variance associated with and without such restraints. As Chapter 5 did not investigate precision without these positioning controls, this comparison could not be made. Results may show that controlling positioning affects measures of hyoid displacement and moreover are unnecessary for reducing variance. Additionally, the application of ultrasound for the assessment of swallowing function requires further exploration. The extent of hyoid displacement is only sufficient in relation to the efficacy of ensuing airway protection and UES opening. Therefore, further research that utilizes ultrasound to document post-treatment changes in hyoid displacement alongside visualisation of other biomechanical events (i.e., with methods such as VFS or FEES) will elucidate the functional relevance of hyoid displacement values obtained with ultrasound.

The results of Chapter 6 suggest advantages of ultrasound over MRI for quantifying CSA of the submental muscles. As for hyoid displacement, participant and transducer stabilization methods may need altering if repeated-measures are required. The treatment study attempted to limit variance introduced by positioning. However, as with hyoid displacement, Chapter 6 did not estimate precision in the absence of these position controls, and therefore comparison of the variance with and without controls remains unknown. Additionally, the effect of the bite-block on submental muscle activation and, therefore, CSA measures needs further investigation to determine if stringent controls are required. Further investigations need to document reliability and precision of ultrasound in quantifying CSA of the submental muscles both with and without position controls, with the time lapse in between assessment sessions representative of the duration of treatment protocols. Once reliability and precision measures are known, responsiveness measures are required by utilizing patient populations to demonstrate the sensitivity of ultrasound to hypertrophy and atrophy. As hypertrophy resulting from neuromuscular exercise has not been documented for the submental muscles, the responsiveness of ultrasound could be explored in other muscle conditions in which magnitude of change is already known. For further insight into the cause of enlarged CSA measures obtained with MRI compared with ultrasound in Chapter 6, repeated CSA measures for both methods would further elucidate sources of variance.

Chapter 7 suggests that reliability of repeated MEP measures was greatest using the ensemble-median waveform for onset latency estimation, and most reliable for area estimation using the rectified average waveform or the mean of 15 individuals. The methods most sensitive to treatment effects, as evidenced by lower within-participant standard deviations were the ensemble-average and ensemble-median waveform for onset latency modifications, and the mean of individual trials for amplitude alterations. This study recorded MEPs from active muscles, as rest MEPs from the submental muscles are problematic. MEPs from other swallowing muscles have been obtained in a rest state and may demonstrate a different response to reliability and precision assessments. The investigation presented in Chapter 7 reflects the results obtained from one rater only. Inter-rater assessment of the same methods would enhance certainty that the cause of the reduction in variance was due to more consistent analysis as opposed to rater preference/bias.

The variance documented for submental MEPs in this research specified precision for group measures as well as within-participants, providing insight into the magnitude of change from repeated-measures at both levels. As mentioned in Section 14.1.1, the group precision estimates from the treatment study were similar to those reported in the Chapter 7. However, the within-participant variance for area measures was much greater in the treatment study than those reported in Chapter 7. This most likely reflects the increased variance introduced by repeating sessions across different days, due to the need to recreate electrode placement and optimal scalp stimulation position. Future investigations need to report the variance associated with patient populations, recreating the situations in which repeated-measures are likely to occur, i.e., across or within the same day. As the within-participant standard deviation estimates from the treatment study varied substantially across the two groups in some cases (see Section 13.3.1.2), the suggestion made in Chapter 8 regarding manometry data may apply to MEP analysis also. It was proposed that incorporating all trials and sessions obtained by manometry may desensitize the measure to any treatment effects, and averaging values obtained from a highly variable individual may not in fact represent the most accurate values. It is possible a similar situation exists with MEPs, with some individuals varying substantially more than others across and within sessions. These highly variable values potentially increase within-participant standard deviations for the group, consequently requiring larger treatment effects. Another crucial area of investigation needed to determine if MEPs provide a feasible method of documenting treatment outcomes is the magnitude of cumulative effects of various

treatments in patient populations. The precision estimates here suggest large magnitude of change is required to exceed variance resulting from repeating MEP assessment alone. This research attempted to deduce the clinical relevance of any adaptations documented in MEPs by simultaneously assessing swallowing biomechanics, however, as no effects of exercise were documented, this functional relationship needs continued investigation in patient populations.

The results presented in Chapter 8 suggest that while there is no evidence of order effects associated with repeated manometry measures, the within-participant variance across both trial and session is considerable. This requires treatment effects, both immediate and cumulative, need to be of sufficient magnitude to surpass this variance. Further research is required to investigate the magnitude of such effects, especially in patient populations for whom treatment change is desired. Additionally, high variance values in the present study were considered to reflect participant and/or catheter placement issues, based on the findings reported in Chapter 8 that stable measures could be obtained for the same sensor in another session, and/or a different sensor in the same session. Insight into the cause of this variance is required to facilitate future studies utilizing manometry. Comparisons of the variance reported for manometry measures in this thesis with variance estimates obtained with circumferential manometric sensors would clarify the effects of radial asymmetry on the current values. As this research only investigated one bolus size (10 mL) of one consistency (water), incorporating various bolus sizes and textures into future studies would quantify additional variance introduced by bolus characteristics. Additionally, repeating the current research alongside radiographs illustrating catheter placement, the influence of catheter position, and individual anatomy on variance estimates could be determined. As similar group standard deviations are reported for manometry in isolation and manofluorography, future studies utilizing manofluorography need to specify within-participant variance to confirm the benefits of utilizing VFS and manometry simultaneously, as proposed by some authors.

The investigation of the separate effects of both effortful-swallowing and modified head-lift revealed no adaptations in swallowing biomechanics or corticobulbar excitability as a result of six weeks of either exercise in healthy older participants. Further research is required to assess the effects of these techniques on swallowing function in patients with dysphagia. As the magnitude of cumulative effects of these exercises on measures such as those utilized in

the current study are unknown, the choice of tools utilized in future investigations needs careful consideration. This is further reinforced by a lack of reliability and precision data available for many measures. Alternative measures to those utilized in the current research, such as assessments of airway protection, may reveal increased responsiveness to the effects of these two neuromuscular exercises. Future research needs to address adaptations associated with rehabilitation techniques at all levels of the swallowing process to provide evidence for these techniques across a variety of impairments. These steps will assist researchers in designing studies adequately powered and structured to detect possible treatment effects, therefore enabling clinicians to be confident in their prescription of dysphagia rehabilitation techniques.



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## **APPENDICES**



## Appendix I: Information sheets and consent forms

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### INFORMATION SHEET

**Research Title:**

Effects of exercise on swallowing.

**Primary Researcher:**

Phoebe Macrae, BSLT  
PhD candidate, Department of Communication Disorders  
University of Canterbury  
Van der Veer Institute for Parkinson's and Brain Research  
66 Stewart St., Christchurch NZ  
(03) 3786 095

**Principal Investigator:**

Maggie-Lee Huckabee, PhD  
Senior lecturer, Department of Communication Disorders  
University of Canterbury  
Van der Veer Institute for Parkinson's and Brain Research  
66 Stewart St., Christchurch NZ  
(03) 378 6070

**Co-Investigator:**

Richard Jones, BE(Hons), ME, PhD, FACPSEM, FIPENZ, SMIEEE, FAIMBE  
Biomedical Engineer & Neuroscientist, Department of Medical Physics and Bioengineering,  
Canterbury District Health Board.  
Van der Veer Institute for Parkinson's and Brain Research  
66 Stewart St., Christchurch NZ  
(03) 3786 077

**Introduction and aims of the project:**

Difficulty with swallowing is a frequent symptom following stroke. Quality of life issues, nutrition and health status are negatively affected for people who are unable to swallow. It is not clearly understood how swallowing rehabilitation techniques improve swallowing, and so investigating the effects of swallowing treatments is necessary in assisting recovery in people with swallowing disorders. This study is part of a PhD research project that will look at how rehabilitation exercises for swallowing changes swallowing muscles, and how the brain communicates with those muscles. This information will assist with planning effective treatment for people suffering from swallowing impairment.

You are invited to participate in a research project that will explore how exercise influences the muscles and the nerves that control swallowing. Interest in participating should be expressed within 2 weeks of the information being provided. You have the right not to participate in the study or subsequently withdraw from this study at any time.

The aim of this project is to provide important information about the influence of two common swallowing exercises on swallowing using measures of how efficiently your nerves communicate with your muscles and how the pressure in your throat changes with muscle strengthening. A fuller understanding of how these techniques influence both nerves and muscles in the swallowing process promises opportunities for improved treatment approaches for swallowing impairment resulting from various brain disorders (e.g., stroke, traumatic brain injury, Parkinson's disease).

**Participant selection:**

Your participation in this study is due to your reply to advertisements or information seminars requesting research participants. Upon your consent, you will complete a questionnaire that will determine your suitability for the study. The study will include 40 participants who have no swallowing problems. Four people from the larger sample of volunteers will be invited to participate in an extension of this study. The extension involves an additional measurement technique at the beginning and the end of the 6-week exercise programme, and is detailed below. In total this study will require approximately 28 hours of your time over 6 weeks (29 if you participate in the extension of this study).



**Exclusion criteria for participants:**

You may not be eligible to participate in this study if you have or ever have had any of the following conditions:

- stroke
- any brain-related condition or any illness that caused brain injury
- any swallowing difficulties
- metal in your head (outside the mouth) such as shrapnel, surgical clips, or fragments from welding or metalwork
- Long-standing history of poorly controlled seizures
- Family history of epilepsy
- implanted devices such as cardiac pacemakers, medical pumps, or intracardiac lines
- frequent or severe headaches
- history of gastroesophageal reflux disorder that has been treated with surgery
- currently pregnant

**Exclusion criteria for those participating in the extension (MRI) section of the study**

- Any metal in the body that has been implanted for less than 6 weeks, such as surgical pins.
- Any metal in the body that is not anchored to bone, such as aneurysm clips, stents.

Completing a questionnaire will ensure that inclusion criteria are met and possible risk factors for participating are identified.

**The research procedure:**

The study involves two assessment sessions at the Van der Veer Institute for Parkinson's and Brain Research and Hagley Radiology, with three sessions if you partake in the extension of this study. In addition to these assessment sessions, you will be required to carry out swallowing exercises for 15 minutes, 3 times per day, 5 days per week for 6 weeks. This totals 45 minutes of exercise a day 5 days a week. Below is a table showing how the time is broken up over the 6 weeks.

Baseline assessment	Exercise period	Outcome assessment
4 hours (4.5 including MRI section of the study, carried out over 2 sessions)	6 weeks. Includes 3 sessions of approximately 15 minutes per day, 5 days per week	2 hours (2.5 including MRI section of the study)

The assessment sessions and the exercise period are described below. If you agree to participate in the study, the following will occur:

1. You will be given an appointment and asked to come to the Swallowing Rehabilitation Research Laboratory at the Van der Veer Institute, 66 Stewart St, Christchurch, New Zealand.
2. A researcher will meet with you at the Van der Veer Institute and you will have an opportunity to have any questions answered. After signing the consent form, you will be asked to complete a standard safety questionnaire to screen for risk of adverse events during one of the procedures. You will also complete a generic questionnaire to ensure inclusion criteria are met and risks are minimised. You will then be seated in a comfortable chair and be ready to begin.

#### **Assessment sessions:**

##### ***I. Motor Evoked Potentials and Electromyography measurements***

3. In each assessment session, the researcher will attach 2 small electrodes to the skin underneath your chin, and 1 to your cheek bone. These will be used to measure muscle activity when you swallow. These electrodes are used only for recording and do not put any electricity into the muscles.
4. Once the electrodes are in place, you will be asked to swallow 10 times, and contract the muscles under your chin as hard as you can 10 times. This is so the strength of your swallows can be determined and will enable the researchers to adjust the equipment to your individual muscle activity during swallowing.
5. Your brain will be stimulated using a technique called transcranial magnetic stimulation (TMS). TMS consists of a figure-of-eight coil that is held over your scalp. When you contract the muscles used for swallowing, the electrical activity in these muscles will trigger this coil to stimulate your brain using a magnetic pulse. This will feel like someone is tapping you on the head but will not hurt. You may also feel a small twitch in the arm opposite the side of the brain being stimulated. When the magnetic pulse is triggered, your brain sends an

electric signal to your swallowing muscles, which can be measured using electrodes placed under your chin. This signal is called a motor evoked potential or MEP.



6. In the first assessment session we will identify which areas of the brain are activated by the magnetic stimulation and how to best apply that stimulation. Starting on the left side of your head, and then moving to the right, several steps need to be taken.
  - a. First, the best area for stimulating brain signals (MEPs) will be identified by measuring MEPs from several places on your scalp and finding which place gives the best response. The researcher will use the magnetic stimulator to find the place on your skull which creates the biggest swallowing signal. During this time you will feel a twitch in the muscles under your chin and a sensation of 'tapping' on your head. Once this area has been determined, the position of the coil will be marked on the scalp using a non-permanent pen.
  - b. Next, we will evaluate how strong the magnetic pulse needs to be to stimulate your brain and what level is best for doing the research. Starting with a very soft 'tap', or magnetic pulse, we will slowly increase the intensity until we determine the lowest level of stimulation required. Then we will increase the intensity until the swallowing signals do not get any larger.
  - c. These steps will be completed on both sides of your head. This will help the researchers identify which side of your brain is involved more in controlling the muscles used for swallowing. All further MEP measurements will be made at the identified location on that side of your brain.
7. Once the area described above has been identified, the researchers will measure MEPs carried out during 15 swallows and 15 repetitions of contracting the muscles under your chin in order

Effects of exercise on swallowing; version 3, 03/09/09

to compare measurements done after you have completed the exercises (head-lift manoeuvre or effortful swallow). While you do this, the researcher will hold the TMS over the part of your skull identified above. Your swallows and muscle contractions will trigger the TMS and you will feel a similar sensation of twitching in your muscles under your chin and light tapping on your head.

## *II. Manometry measurements*

8. You will be given a demonstration and directions about how to perform an effortful swallow, which requires you to swallow hard using all the muscles in your mouth and throat.
9. After this instructional period, a small tube will be carefully inserted through one side of your nose. This tube is about the size of a piece of spaghetti and is very soft and flexible. As soon as the tube reaches the back of your throat, you will be required to look up to the ceiling briefly while the tube turns the corner into your upper throat. You will then be handed a glass of water and asked to continuously and comfortably drink the water through a straw. In doing so, the tube will be swallowed into the upper oesophagus.
10. The tube will then be slowly pulled upwards until correct placement is assured in the throat. Once in the correct place, a small piece of first aid tape will be wrapped around the tube and secured on your nose to ensure the tube does not move while you swallow.
11. Imbedded in the tube are three manometric pressure sensors that measure pressure in the throat. The pictures below show how the tube will be inserted through the nose and positioned once it is in the correct place. The x-ray picture at the end is an example only, as no x-ray images will be taken during this study.



12. You will be asked to complete 5 repetitions of 3 different types of swallows: regular saliva swallows, effortful swallows, and 10-ml water swallows.

13. The tube will then be removed and you will be ready for the next assessment procedure.

### ***III. Ultrasound measurements***

14. You will be seated in a comfortable chair in an examination room at Hagley Radiology (this is located on the ground level of the Van der Veer Institute Building).
15. An imprint of your teeth will be made using soft putty on a bite-block. You will be asked to bite down on your back teeth and hold the bite-block in place for approximately 1 minute while the putty sets.
16. The bite-block will then be removed and attached to the moveable arm of the placement stand. The placement stand will be adjusted so that you can position the bite-block comfortably in your mouth from your seated position.
17. A clear conductive jelly will be put on the skin under your chin to allow imaging of the muscles. The ultrasound transducer (the imaging tool) will be lightly placed under your chin.
18. You will be asked to remain very still and relaxed during the first part of the ultrasound imaging procedure. For the second part you will be asked to swallow 5 times, at a rate that is comfortable for you. During these procedures, you will not feel anything unusual or experience any discomfort. Ultrasound procedures should take no more than 20 minutes.

### ***IV. Magnetic resonance imaging (MRI) - optional***

19. If you agree to take part in the extended section of this study, you will also have a structural magnetic resonance imaging scan. This will be done on a separate day to the manometry and motor evoked potentials part of your first session. It will be completed on the same day as your ultrasound imaging, and will also be carried out at Hagley Radiology.

20. You will lie down on the table of the MRI scanner and a head-piece will be attached to the table you are lying on. This head-piece is close fitting and contains the magnetic coils required to produce the images of your muscles in your throat.
21. The table will then be moved into the MRI scanner and the researcher will communicate with you through a microphone. A microphone in the scanner will allow the researcher to hear you from outside the scanner.
22. Once you are comfortable, the researcher will ask you to hold as still as you can for approximately 5 minutes. Once you are ready, the scan will start and you will hear a series of loud clicks and hums. The scan will allow the researcher to measure the size (volume) of the muscles under your chin that are used for effective swallowing. The scan will last for approximately 5 minutes. The table will then be removed from the scanner and you will be finished with the MRI section of the study.

#### *V. Exercise demonstration*

23. Once your assessment session is completed, you will be given instructions on how to complete one of two swallowing exercises: effortful swallow or head-lift manoeuvre. You will carry out your first exercise session in the swallowing rehabilitation research laboratory. The instructions will vary depending on which exercise group you are assigned to:
  - a. *Effortful swallow*: You will have two electrodes placed under your chin and one on your jaw bone (see step 4). These electrodes will record the activity of your muscles under the chin. You will not be able to see this screen but the researcher will use it to provide you with verbal feedback about the strength of your swallows. You will then be instructed to swallow your saliva normally. For the next swallow, you will be asked to “swallow hard with all the muscles in your mouth and throat”. You will receive verbal feedback and encouraged to swallow harder until an appropriate increase in muscle strength is seen. Effortful swallow will be carried out 33 times
  - b. *Head-lift manoeuvre*: You will lie supine on a padded bench with your arms by your sides and your head flat on the bench. You will then raise your head up briefly to visualize your toes and then relax your head back down onto the bench. You will do this thirty times. You will then lift your head to see your toes and hold it for 30

seconds, or for as long as is comfortable. This sustained head-lift will be repeated 3 times.

24. Following the exercise practice, you will be given the chance to ask any questions or clarify any aspect of the exercise you don't understand. You will be given a weekly log sheet and the researcher will show you how to fill it in. You will use this log sheet at home to record when you carry out the exercises and can also make comments regarding any difficulties you experience each time you carry them out.
25. At 30, 60 and 90 minute intervals in this first exercise session only, you will undergo repeated assessment of how quickly your nerves send information to the muscles: the MEP assessment. This will be done exactly as is described in step 7.

#### ***VI. Exercise programme***

26. For 6 weeks following your assessment session, you will be required to complete the swallowing exercise you practised after the assessment session (either effortful swallow or head-lift manoeuvre) 3 times per day, 5 days per week. Each daily session should take no more than 15 minutes and involve 33 repetitions of effortful swallow or 30 repetitions of brief head-lifts and 3 sustained head-lifts. You will be required to record each session on your weekly log sheet.
27. The researcher will arrange a time that is suitable for you to visit you at home once per week. Alternatively, if you would prefer to come to the Van der Veer Institute for these sessions, a time that suits you to do this can also be arranged. These sessions will follow the same procedure as step 19.

#### ***Outcome measurements***

28. On the day following completion of your 6-week exercise programme, you will be required to attend another assessment session at the Van der Veer Institute at a time that suits you. The procedure for this session will be the same as that described in steps 3-5 and 8-18.

29. The whole research project should take approximately 28 hours of your time, over 6 weeks.
30. We may not be able to measure MEPs in all volunteers. This is because every brain is slightly different. The procedures explained under point 6a – 6c will help us identify if we can use the data recorded from your brain for our study. Should we not be able to use your data for our study, you will not have to return for the other 2 sessions, or complete the exercise programme at home. You will still be reimbursed \$20 for your participation in the first part of this assessment session.

#### **Risks and Benefits:**

Single-pulse TMS, as applied in this study, is considered to carry no risk beyond occasionally causing local discomfort at the site of stimulation and headaches that last for a short while in subjects who are prone to headache. Caution is advised when stimulating participants with a history of seizures, and therefore participants with a long-standing history of poorly controlled seizures or a family history of seizures will be excluded from participating. MRI carries risk for those with newly implanted surgical pins, or metal that is not anchored in bone (e.g., stents and aneurysm clips), and therefore volunteers with such material in their body will be excluded from participating. Completing the safety questionnaire will ensure any potential risks of you participating are identified.

For participants enrolled in the study, there are no direct benefits to you as an individual although you will receive \$70 as reimbursement for travel expenses. You will be part of a study that contributes important information on how exercise influences the nerves and muscles that control swallowing. This information will, in turn, assist with the development of improved treatment techniques for swallowing disorders.

Though not expected, you will be monitored very carefully by the researchers for any negative outcomes arising from your participation in this study. The Van der Veer Institute has equipment for dealing with medical emergencies.

#### **Participation:**

If you agree to take part in this study, you are free to withdraw at any time, without having to give a reason.



**Confidentiality:**

Research findings will be presented at international research meetings and submitted for publication in peer reviewed journals. Additionally, research findings will be made available to the local Canterbury medical community through research presentations and regional forums. However, no material which could personally identify you will be used in any reports on this study. Consent forms will be kept in a locked filing cabinet in the locked Swallowing Research Laboratory or will be stored on password-protected laboratory computers. Research data will be stored for a period of ten years after data collection is complete, at which time they will be destroyed. With your permission, data from this study may be used in future related studies, which have been given ethical approval from a Health & Disability Ethics Committee

**Results:**

If requested, you will be offered copies of the publications that arise from this research. However, you should be aware that a significant delay may occur between completion of data collection and completion of the final report. Alternatively, or in addition, you can choose to have the results of the study discussed with you personally by the lead investigator.

**Compensation:**

In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Injury Prevention, Rehabilitation and Compensation Act. ACC cover is not automatic and your case will need to be assessed by ACC according to the provisions of the 2002 Injury Prevention Rehabilitation and Compensation Act. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators.

If you have any questions about ACC, contact your nearest ACC office or the investigator.

**Questions:**

You may have a friend, family, or whanau support to help you understand the risks and/or benefits of this study and any other explanation you may require.

Please contact the primary researcher, Phoebe Macrae, if you require any further information about the study. Phoebe can be contacted during work hours at (03) 378-6095 or after hours on 027 210 6280.

If you need an interpreter, this can be provided.

If you have any queries or concerns about your rights as a participant in this study, you may wish to contact a Health and Disability Advocate, telephone:

South Island 0800 377 766 or (03) 377 7501 in Christchurch. Free Fax (NZ wide): 0800 2787 7678 (08002SUPPORT) Email (NZ wide): [advocacy@hdc.org.nz](mailto:advocacy@hdc.org.nz)

This study has received ethical approval from the Upper South B Regional Ethics Committee.

## INFORMATION SHEET

**Research Title:**

**Pressures in the throat during swallowing**

**Primary Researcher:**

Phoebe Macrae, BSLT  
PhD candidate, Department of Communication Disorders  
University of Canterbury  
Van der Veer Institute for Parkinson's and Brain Research  
66 Stewart St., Christchurch NZ  
(03) 3786 095

**Principal Investigator:**

Maggie-Lee Huckabee, PhD  
Senior lecturer, Department of Communication Disorders  
University of Canterbury  
Van der Veer Institute for Parkinson's and Brain Research  
66 Stewart St., Christchurch NZ  
(03) 378 6070

**Co-Investigator:**

Richard Jones, BE(Hons), ME, PhD, FACPSEM, FIPENZ, SMIEEE, FAIMBE  
Biomedical Engineer & Neuroscientist, Department of Medical Physics and Bioengineering,  
Canterbury District Health Board.  
Van der Veer Institute for Parkinson's and Brain Research  
66 Stewart St., Christchurch NZ  
(03) 3786 077

**Introduction and aims of the project:**

This study will look at how consistently the pressure in your throat during swallowing is measured across three sessions. This study is part of a PhD research project. If you need an interpreter, this can be provided.

You are invited to participate in a research project that will explore how hard the muscles in your throat work during swallowing, and how consistently this muscle effort is measured. Interest in participating should be expressed within 2 weeks of the information being provided. You have the right not to participate in the study or subsequently withdraw from this study at any time.

The aim of this project is to provide important information about a technique used in diagnosing swallowing disorders. Swallowing disorders can occur as a result of stroke, or other neurological conditions such as Parkinson's or Huntington's disease. By refining the way we use this diagnostic tool, we can be more precise with our use of the technique when investigating swallowing disorders in research.

**Participant selection:**

Your participation in this study is due to your reply to advertisements requesting research participants. Upon your consent, you will complete a questionnaire that will determine your suitability for the study. The study will include 20 healthy participants over the age of 18 years. In total this study will require approximately 90 minutes of your time completed in 1, 2 or 3 sessions (3 x 30 minute blocks).

**Exclusion criteria:**

You may not be eligible to participate in this study if you have or ever have had any of the following conditions:

- stroke
- any brain-related condition or any illness that caused brain injury
- any swallowing difficulties

Completing a questionnaire will ensure that inclusion criteria are met and possible risk factors for participating are identified.

**The research procedure:**

The study involves 1, 2 or 3 sessions at the Van der Veer Institute for Parkinson's and Brain Research and Hagley Radiology. How many sessions you come for is up to you. In total you will be required for approximately 90 minutes. The procedure (detailed below) will be carried out 3 times. These can be done all on the same day (1 session), or over separate days (2 or 3 sessions)

The procedure is described below. If you agree to participate in the study, the following will occur:

1. You will be given an appointment and asked to come to the Swallowing Rehabilitation Research Laboratory at the Van der Veer Institute, 66 Stewart St, Christchurch, New Zealand.
2. A researcher will meet with you at the Van der Veer Institute and you will have an opportunity to have any questions answered. After signing the consent form, you will be asked to complete generic questionnaire to ensure inclusion criteria are met and risks are minimised. You will then be seated in a comfortable chair and be ready to begin the research.

**I. *Manometry procedure***

3. A small tube will be carefully inserted through one side of your nose. This tube is about the size of a piece of spaghetti and is very soft and flexible. As soon as the tube reaches the back of your throat, you will be required to look up to the ceiling briefly while the tube turns the corner into your upper throat. You can then return your head to a comfortable position before being handed a glass of water and asked to continuously and comfortably drink the water through a straw. In doing so, the tube will be swallowed into the upper esophagus.
4. The tube will then be slowly pulled upwards until correct placement is assured in the throat. Once in the correct place, a small piece of first aid tape will be wrapped around the tube and secured on your nose to ensure the tube does not move while you swallow. Imbedded in the tube are three pressure sensors that measure how hard the muscles in your throat move during a swallow.
5. You will be asked to complete 5 repetitions of 2 different types of swallows: regular saliva swallows, and 10-ml water swallows. This will take approximately 5 minutes.

6. The tube will then be removed and sterilized for 15-20 minutes while you wait. You will be free to read a magazine/book during this time.
7. Once sterilization is complete, steps 3-6 will be completed another two times.
8. The whole research project should take approximately 90 minutes of your time.

**Risks and Benefits:**

Manometry, or insertion of the small tube through the nose into the throat poses no physical risk beyond the slight risk of nose bleed and minor discomfort. Placement of the tube, although not comfortable, is not a painful procedure and is tolerated well by most participants. You may withdraw from the study at any time you feel the procedures are breaching your tolerable comfort level.

There are no direct benefits to you as an individual. You will be part of a study that contributes important information on how the muscles in the throat contract during swallowing. This information will, in turn, assist with the more precise use of manometry in swallowing research.

Though not expected, you will be monitored very carefully by the researchers for any negative outcomes arising from your participation in this study. The Van der Veer Institute has equipment for dealing with medical emergencies.

**Participation:**

If you do agree to take part in the study, you are free to withdraw from the study at any time, without having to give a reason, and this will in no way affect your academic progress.

**Confidentiality:**

Research findings will be presented at international research meetings and submitted for publication in peer reviewed journals. Additionally, research findings will be made available to the local Canterbury medical community through research presentations and regional forums. However, no material which could personally identify you will be used in any reports on this study. Consent forms will be kept in a locked filing cabinet in the locked Swallowing Research Laboratory or will be stored on password-protected laboratory computers. Research data will be stored for a period of ten years after data collection is complete, at which time they will be destroyed. With your permission, data from this study may be used in future related studies, which have been given ethical approval from a Health & Disability Ethics Committee

**Results:**

If requested, you will be offered copies of the publications that arise from this research. However, you should be aware that a significant delay may occur between completion of data collection and completion of the final report. Alternatively, or in addition, you can choose to have the results of the study discussed with you personally by the lead investigator.

**Compensation:**

In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Injury Prevention, Rehabilitation and Compensation Act. ACC cover is not automatic and your case will need to be assessed by ACC according to the provisions of the 2002 Injury Prevention Rehabilitation and Compensation Act. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators.

If you have any questions about ACC, contact your nearest ACC office or the investigator.

**Questions:**

You may have a friend, family, or whanau support to help you understand the risks and/or benefits of this study and any other explanation you may require.

Please contact the primary researcher, Phoebe Macrae, if you require any further information about the study. Phoebe can be contacted during work hours at (03) 378-6098 or after hours on 027 210 6280.

If you have any queries or concerns regarding your rights as a participant in this study, you may wish to contact an independent health and disability advocate: Free phone: 0800 555 050 Free fax: 0800 2 SUPPORT (0800 2787 7678) Email: [advocacy@hdc.org.nz](mailto:advocacy@hdc.org.nz)

This study has received ethical approval from the Upper South A Regional Ethics Committee.

## INFORMATION SHEET

**Research Title:**

**Effects of exercise on swallowing.**

**Primary Researcher:**

Phoebe Macrae, BSLT  
PhD candidate, Department of Communication Disorders  
University of Canterbury  
Van der Veer Institute for Parkinson's and Brain Research  
66 Stewart St., Christchurch NZ  
(03) 3786 095

**Principal Investigator:**

Maggie-Lee Huckabee, PhD  
Senior lecturer, Department of Communication Disorders  
University of Canterbury  
Van der Veer Institute for Parkinson's and Brain Research  
66 Stewart St., Christchurch NZ  
(03) 378 6070

**Co-Investigator:**

Richard Jones, BE(Hons), ME, PhD, FACPSEM, FIPENZ, SMIEEE, FAIMBE  
Biomedical Engineer & Neuroscientist, Department of Medical Physics and Bioengineering,  
Canterbury District Health Board.  
Van der Veer Institute for Parkinson's and Brain Research  
66 Stewart St., Christchurch NZ  
(03) 3786 077



**Introduction and aims of the project:**

Difficulty with swallowing is a frequent symptom following stroke. Quality of life issues, nutrition and health status are negatively affected for people who are unable to swallow. It is not clearly understood how swallowing rehabilitation techniques improve swallowing, and so investigating the effects of swallowing treatments is necessary in assisting recovery in people with swallowing disorders. This study is part of a PhD research project that will look at how rehabilitation exercises for swallowing changes swallowing muscles, and how the brain communicates with those muscles. This information will assist with planning effective treatment for people suffering from swallowing impairment.

You are invited to participate in a research project that will explore how exercise influences the muscles and the nerves that control swallowing. Interest in participating should be expressed within 2 weeks of the information being provided. You have the right not to participate in the study or subsequently withdraw from this study at any time.

The aim of this project is to provide important information about the influence of two common swallowing exercises on swallowing using measures of how efficiently your nerves communicate with your muscles and how the pressure in your throat changes with muscle strengthening. A fuller understanding of how these techniques influence both nerves and muscles in the swallowing process promises opportunities for improved treatment approaches for swallowing impairment resulting from various brain disorders (e.g., stroke, traumatic brain injury, Parkinson's disease).

**Participant selection:**

Your participation in this study is due to your reply to advertisements or information seminars requesting research participants. Upon your consent, you will complete a questionnaire that will determine your suitability for the study. The study will include 40 participants who have no swallowing problems. In total this study will require approximately 28 hours of your time over 6 weeks.

**Exclusion criteria for participants:**

You may not be eligible to participate in this study if you have or ever have had any of the following conditions:

- stroke
- any brain-related condition or any illness that caused brain injury
- any swallowing difficulties
- metal in your head (outside the mouth) such as shrapnel, surgical clips, or fragments from welding or metalwork
- Long-standing history of poorly controlled seizures
- Family history of epilepsy
- implanted devices such as cardiac pacemakers, medical pumps, or intracardiac lines
- frequent or severe headaches
- history of gastroesophageal reflux disorder that has been treated with surgery
- currently pregnant

Completing a questionnaire will ensure that inclusion criteria are met and possible risk factors for participating are identified.

#### **The research procedure:**

The study involves two assessment sessions at the Van der Veer Institute for Parkinson's and Brain Research and Hagley Radiology. In addition to these assessment sessions, you will be required to carry out swallowing exercises for 15 minutes, 3 times per day, 5 days per week for 6 weeks. This totals 45 minutes of exercise a day 5 days a week. Below is a table showing how the time is broken up over the 6 weeks.

Baseline assessment	Exercise period	Outcome assessment
4 hours	6 weeks. Includes 3 sessions of approximately 15 minutes per day, 5 days per week	2 hours

The assessment sessions and the exercise period are described below. If you agree to participate in the study, the following will occur:

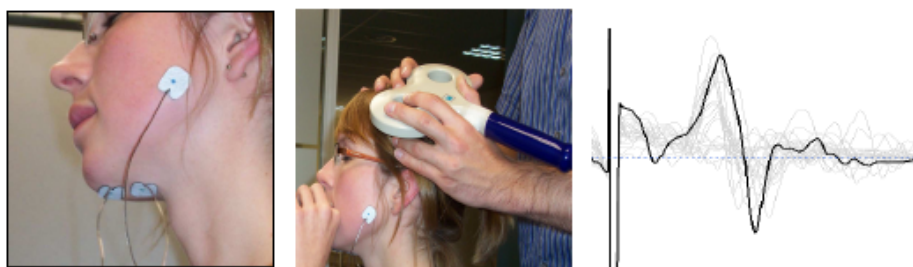
1. You will be given an appointment and asked to come to the Swallowing Rehabilitation Research Laboratory at the Van der Veer Institute, 66 Stewart St, Christchurch, New Zealand.

2. A researcher will meet with you at the Van der Veer Institute and you will have an opportunity to have any questions answered. After signing the consent form, you will be asked to complete a standard safety questionnaire to screen for risk of adverse events during one of the procedures. You will also complete a generic questionnaire to ensure inclusion criteria are met and risks are minimised. You will then be seated in a comfortable chair and be ready to begin.

#### **Assessment sessions:**

##### ***I. Motor Evoked Potentials and Electromyography measurements***

3. In each assessment session, the researcher will attach 2 small electrodes to the skin underneath your chin, and 1 to your cheek bone. These will be used to measure muscle activity when you swallow. These electrodes are used only for recording and do not put any electricity into the muscles.
4. Once the electrodes are in place, you will be asked to swallow 10 times, and contract the muscles under your chin as hard as you can 10 times. This is so the strength of your swallows can be determined and will enable the researchers to adjust the equipment to your individual muscle activity during swallowing.
5. Your brain will be stimulated using a technique called transcranial magnetic stimulation (TMS). TMS consists of a figure-of-eight coil that is held over your scalp. When you contract the muscles used for swallowing, the electrical activity in these muscles will trigger this coil to stimulate your brain using a magnetic pulse. This will feel like someone is tapping you on the head but will not hurt. You may also feel a small twitch in the arm opposite the side of the brain being stimulated. When the magnetic pulse is triggered, your brain sends an electric signal to your swallowing muscles, which can be measured using electrodes placed under your chin. This signal is called a motor evoked potential or MEP.

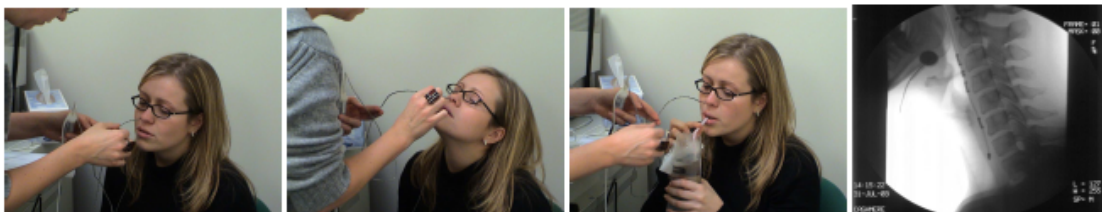


6. In the first assessment session we will identify which areas of the brain are activated by the magnetic stimulation and how to best apply that stimulation. Starting on the left side of your head, and then moving to the right, several steps need to be taken.
  - a. First, the best area for stimulating brain signals (MEPs) will be identified by measuring MEPs from several places on your scalp and finding which place gives the best response. The researcher will use the magnetic stimulator to find the place on your skull which creates the biggest swallowing signal. During this time you will feel a twitch in the muscles under your chin and a sensation of 'tapping' on your head. Once this area has been determined, the position of the coil will be marked on the scalp using a non-permanent pen.
  - b. Next, we will evaluate how strong the magnetic pulse needs to be to stimulate your brain and what level is best for doing the research. Starting with a very soft 'tap', or magnetic pulse, we will slowly increase the intensity until we determine the lowest level of stimulation required. Then we will increase the intensity until the swallowing signals do not get any larger.
  - c. These steps will be completed on both sides of your head. This will help the researchers identify which side of your brain is involved more in controlling the muscles used for swallowing. All further MEP measurements will be made at the identified location on that side of your brain.
7. Once the area described above has been identified, the researchers will measure MEPs carried out during 15 swallows and 15 repetitions of contracting the muscles under your chin in order to compare measurements done after you have completed the exercises (head-lift manoeuvre or effortful swallow). While you do this, the researcher will hold the TMS over the part of your skull identified above. Your swallows and muscle contractions will trigger the TMS and

you will feel a similar sensation of twitching in your muscles under your chin and light tapping on your head.

## ***II. Manometry measurements***

8. You will be given a demonstration and directions about how to perform an effortful swallow, which requires you to swallow hard using all the muscles in your mouth and throat.
9. After this instructional period, a small tube will be carefully inserted through one side of your nose. This tube is about the size of a piece of spaghetti and is very soft and flexible. As soon as the tube reaches the back of your throat, you will be required to look up to the ceiling briefly while the tube turns the corner into your upper throat. You will then be handed a glass of water and asked to continuously and comfortably drink the water through a straw. In doing so, the tube will be swallowed into the upper oesophagus.
10. The tube will then be slowly pulled upwards until correct placement is assured in the throat. Once in the correct place, a small piece of first aid tape will be wrapped around the tube and secured on your nose to ensure the tube does not move while you swallow.
11. Imbedded in the tube are three manometric pressure sensors that measure pressure in the throat. The pictures below show how the tube will be inserted through the nose and positioned once it is in the correct place. The x-ray picture at the end is an example only, as no x-ray images will be taken during this study.



12. You will be asked to complete 5 repetitions of 3 different types of swallows: regular saliva swallows, effortful swallows, and 10-ml water swallows.
13. The tube will then be removed and you will be ready for the next assessment procedure.

### *III. Ultrasound measurements*

14. You will be seated in a comfortable chair in an examination room at Hagley Radiology (this is located on the ground level of the Van der Veer Institute Building).
15. An imprint of your teeth will be made using soft putty on a bite-block. You will be asked to bite down on your back teeth and hold the bite-block in place for approximately 1 minute while the putty sets.
16. The bite-block will then be removed and attached to the moveable arm of the placement stand. The placement stand will be adjusted so that you can position the bite-block comfortably in your mouth from your seated position.
17. A clear conductive jelly will be put on the skin under your chin to allow imaging of the muscles. The ultrasound transducer (the imaging tool) will be lightly placed under your chin.
18. You will be asked to remain very still and relaxed during the first part of the ultrasound imaging procedure. For the second part you will be asked to swallow 5 times, at a rate that is comfortable for you. During these procedures, you will not feel anything unusual or experience any discomfort. Ultrasound procedures should take no more than 20 minutes.

### *IV. Exercise demonstration*

19. Once your assessment session is completed, you will be given instructions on how to complete one of two swallowing exercises: effortful swallow or head-lift manoeuvre. You will carry out your first exercise session in the swallowing rehabilitation research laboratory. The instructions will vary depending on which exercise group you are assigned to:
  - a. *Effortful swallow*: You will have two electrodes placed under your chin and one on your jaw bone (see step 4). These electrodes will record the activity of your muscles under the chin. You will not be able to see this screen but the researcher will use it to provide you with verbal feedback about the strength of your swallows. You will then be instructed to swallow your saliva normally. For the next swallow, you will be asked to “swallow hard with all the muscles in your mouth and throat”. You will

receive verbal feedback and encouraged to swallow harder until an appropriate increase in muscle strength is seen. Effortful swallow will be carried out 33 times

- b. *Head-lift manoeuvre:* You will lie supine on a padded bench with your arms by your sides and your head flat on the bench. You will then raise your head up briefly to visualize your toes and then relax your head back down onto the bench. You will do this thirty times. You will then lift your head to see your toes and hold it for 30 seconds, or for as long as is comfortable. This sustained head-lift will be repeated 3 times.

- 20. Following the exercise practice, you will be given the chance to ask any questions or clarify any aspect of the exercise you don't understand. You will be given a weekly log sheet and the researcher will show you how to fill it in. You will use this log sheet at home to record when you carry out the exercises and can also make comments regarding any difficulties you experience each time you carry them out.
- 21. At 30, 60 and 90 minute intervals in this first exercise session only, you will undergo repeated assessment of how quickly your nerves send information to the muscles: the MEP assessment. This will be done exactly as is described in step 7.

## *V. Exercise programme*

- 22. For 6 weeks following your assessment session, you will be required to complete the swallowing exercise you practised after the assessment session (either effortful swallow or head-lift manoeuvre) 3 times per day, 5 days per week. Each daily session should take no more than 15 minutes and involve 33 repetitions of effortful swallow or 30 repetitions of brief head-lifts and 3 sustained head-lifts. You will be required to record each session on your weekly log sheet.
- 23. The researcher will arrange a time that is suitable for you to visit you at home once per week. Alternatively, if you would prefer to come to the Van der Veer Institute for these sessions, a time that suits you to do this can also be arranged. These sessions will follow the same procedure as step 19.

### *Outcome measurements*

24. On the day following completion of your 6-week exercise programme, you will be required to attend another assessment session at the Van der Veer Institute at a time that suits you. The procedure for this session will be the same as that described in steps 3-5 and 8-18.
25. The whole research project should take approximately 28 hours of your time, over 6 weeks.
26. We may not be able to measure MEPs in all volunteers. This is because every brain is slightly different. The procedures explained under point 6a – 6c will help us identify if we can use the data recorded from your brain for our study. Should we not be able to use your data for our study, you will not have to return for the other 2 sessions, or complete the exercise programme at home. You will still be reimbursed \$20 for your participation in the first part of this assessment session.

### **Risks and Benefits:**

Single-pulse TMS, as applied in this study, is considered to carry no risk beyond occasionally causing local discomfort at the site of stimulation and headaches that last for a short while in subjects who are prone to headache. Caution is advised when stimulating participants with a history of seizures, and therefore participants with a long-standing history of poorly controlled seizures or a family history of seizures will be excluded from participating. Completing the safety questionnaire will ensure any potential risks of you participating are identified.

For participants enrolled in the study, there are no direct benefits to you as an individual although you will receive \$70 as reimbursement for travel expenses. You will be part of a study that contributes important information on how exercise influences the nerves and muscles that control swallowing. This information will, in turn, assist with the development of improved treatment techniques for swallowing disorders.

Though not expected, you will be monitored very carefully by the researchers for any negative outcomes arising from your participation in this study. The Van der Veer Institute has equipment for dealing with medical emergencies.



**Participation:**

If you agree to take part in this study, you are free to withdraw at any time, without having to give a reason.

**Confidentiality:**

Research findings will be presented at international research meetings and submitted for publication in peer reviewed journals. Additionally, research findings will be made available to the local Canterbury medical community through research presentations and regional forums. However, no material which could personally identify you will be used in any reports on this study. Consent forms will be kept in a locked filing cabinet in the locked Swallowing Research Laboratory or will be stored on password-protected laboratory computers. Research data will be stored for a period of ten years after data collection is complete, at which time they will be destroyed. With your permission, data from this study may be used in future related studies, which have been given ethical approval from a Health & Disability Ethics Committee

**Results:**

If requested, you will be offered copies of the publications that arise from this research. However, you should be aware that a significant delay may occur between completion of data collection and completion of the final report. Alternatively, or in addition, you can choose to have the results of the study discussed with you personally by the lead investigator.

**Compensation:**

In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Injury Prevention, Rehabilitation and Compensation Act. ACC cover is not automatic and your case will need to be assessed by ACC according to the provisions of the 2002 Injury Prevention Rehabilitation and Compensation Act. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators.

If you have any questions about ACC, contact your nearest ACC office or the investigator.

**Questions:**

You may have a friend, family, or whanau support to help you understand the risks and/or benefits of this study and any other explanation you may require.

Please contact the primary researcher, Phoebe Macrae, if you require any further information about the study. Phoebe can be contacted during work hours at (03) 378-6095 or after hours on 027 210 6280.

If you need an interpreter, this can be provided.

If you have any queries or concerns about your rights as a participant in this study, you may wish to contact a Health and Disability Advocate, telephone:

South Island 0800 377 766 or (03) 377 7501 in Christchurch. Free Fax (NZ wide): 0800 2787 7678 (08002SUPPORT) Email (NZ wide): [advocacy@hdc.org.nz](mailto:advocacy@hdc.org.nz)

This study has received ethical approval from the Upper South B Regional Ethics Committee.

**CONSENT FORM**

**Pressures in the throat during swallowing.**

English	I wish to have an interpreter.	Yes	No
Maori	E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero.	Ae	Kao
Samoan	Ou te mana'o ia iai se fa'amatala upu.	Ioe	Leai
Tongan	Oku ou fiema'u ha fakatonulea.	Io	Ikai
Cook Island	Ka inangaro au i tetai tangata uri reo.	Ae	Kare
Fijian	Au gadreva me dua e vakadewa vosa vei au	Io	Sega
Tokelaun	Ko au e fofou ki he tino ke fakaliliu te gagana Peletania ki na gagana o na motu o te Pahefika	Ioe	Leai
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu.	E	Nakai

I have read and I understand the Information Sheet dated 10.06.2010 for volunteers taking part in the study designed to evaluate how the muscles of the throat contract during swallowing. I have had the opportunity to discuss this study. I am satisfied with the answers I have been given.

I have had the opportunity to use whanau support or a friend to help me ask questions and understand the study

I understand that taking part in this study is voluntary (my choice), and that I may withdraw from the study at any time, and, if applicable, this will in no way affect my academic progress. I understand that if I choose to withdraw from the study, I may also withdraw all information that I have provided.

I understand that the information obtained from this research may be published. However, I understand that my participation in this study is confidential and that no material which could identify me will be used in any reports on this study.

I understand that the investigation will be stopped if it should appear harmful to me and I know whom to contact if I have any side effects to the study or have any questions about the study.

I understand there are potential risks of participation in the study as explained to me by the researcher. I have filled out the questionnaire, and I feel confident that none of the risk factor outlined in the questionnaire apply to me.

I consent to the use of my data for future related studies, which have been given ethical approval from a Health and Disability Ethics Committee.

I have had time to consider whether to take part.

I wish to receive a copy of the results.

YES / NO

\* Please note that a significant delay may occur between data collection and publication of the results

I, \_\_\_\_\_, (*full name*) hereby consent to take part in this study

Date:

Signature:

Full names of researcher:

Contact phone number for researcher:

Project explained by:

Signature:

Date:

(Note: A copy of the consent form to be retained by participant)

**CONSENT FORM**

**Effects of exercise on swallowing.**

English	I wish to have an interpreter.	Yes	No
Maori	E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero.	Ae	Kao
Samoan	Ou te mana'o ia iai se fa'amatala upu.	Ioe	Leai
Tongan	Oku ou fiema'u ha fakatonulea.	Io	Ikai
Cook Island	Ka inangaro au i tetai tangata uri reo.	Ae	Kare
Fijian	Au gadreva me dua e vakadewa vosa vei au	Io	Sega
Tokelaun	Ko au e fofou ki he tino ke fakaliliu te gagana Peletania ki na gagana o na motu o te Pahefika	Ioe	Leai
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu.	E	Nakai

I have read and I understand the Information Sheet dated 04-02-09 for volunteers taking part in the study designed to evaluate the effect of neuromuscular exercise on how the brain controls swallowing. I have had the opportunity to discuss this study. I am satisfied with the answers I have been given.

I have had the opportunity to use whanau support or a friend to help me ask questions and understand the study

I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time. I understand that if I choose to withdraw from the study, I may also withdraw all information that I have provided.

I understand that the information obtained from this research may be published. However, I understand that my participation in this study is confidential and that no material which could identify me will be used in any reports on this study.

I understand that the investigation will be stopped if it should appear harmful to me and I know whom to contact if I have any side effects to the study or have any questions about the study.

I understand there are potential risks of participation in the study as explained to me by the researcher. I have filled out the questionnaire, and I feel confident that none of the risk factor outlined in the questionnaire apply to me.

I consent to the use of my data for future related studies, which have been given ethical approval from a Health and Disability Ethics Committee.

I understand the compensation provisions for this study.

I have had time to consider whether to take part.

I wish to receive a copy of the results YES / NO

\* Please note that a significant delay may occur between data collection and publication of the results

I would like the researcher to discuss the outcomes of the study with me YES / NO

I, \_\_\_\_\_ hereby consent to take part in this study.

Signature \_\_\_\_\_ Date \_\_\_\_\_

Signature of researcher: \_\_\_\_\_

Name of researcher: Phoebe Macrae

Name of primary researcher and contact phone numbers:

Phoebe Macrae

Work ph. 03 378-6095

Mobile ph. 027 210 6280

(Note: A copy of the consent form to be retained by participant)

Effects of exercise on swallowing; version 2; 04/02/09

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## Appendix II: Treatment study questionnaire



### QUESTIONNAIRE

#### Effects of exercise on swallowing.

Identifying number: \_\_\_\_\_

Age: \_\_\_\_\_

Which ethnic group do you belong to:

- |   |  |
|---|--|
| <input type="checkbox"/> New Zealand European | <input type="checkbox"/> New Zealand Maori |
| <input type="checkbox"/> Samoan               | <input type="checkbox"/> Cook Island Maori |
| <input type="checkbox"/> Tongan               | <input type="checkbox"/> Niuean            |
| <input type="checkbox"/> Chinese              | <input type="checkbox"/> Indian            |
| <input type="checkbox"/> Other _____          |  |

Please complete the following questionnaire by ticking the box that is most applicable to you.

- ☐ Stroke
- ☐ Swallowing difficulties
- ☐ Head and/or neck injury
- ☐ Head/ and/or neck surgery
- ☐ Neurological disorders (e.g. Multiple Sclerosis etc.)
- ☐ Gastroesophageal Reflux Disease
- ☐ Family history of epilepsy
- ☐ Long standing history of poorly controlled seizures
- ☐ Muscular disease (e.g., Muscular atrophy)
- ☐ Metal in your head (outside the mouth) such as shrapnel, surgical clips, or fragments from welding or metalwork
- ☐ Implanted devices such as cardiac pacemakers, medical pumps, or intracardiac lines
- ☐ Frequent or severe headaches
- ☐ Currently pregnant

Are you currently taking any medications that may affect your swallowing?

Yes / No (Please circle one)

If yes, please describe

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Do you have any other medical problems which you feel may impact on your ability to participate (e.g., inability to understand instructions)?

Yes / No      (Please circle one)

If yes, please describe

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## Appendix III: Exercise record sheet – Effortful-swallowing group

I.D.		Effortful swallow log sheet		
		TIME OF DAY		
		Morning	Afternoon	Evening
<b>DAYS</b>	<b>Monday</b>	Reps Mins	Reps Mins	Reps Mins
	<b>Tuesday</b>	Reps Mins	Reps Mins	Reps Mins
	<b>Wednesday</b>	Reps Mins	Reps Mins	Reps Mins
	<b>Thursday</b>	Reps Mins	Reps Mins	Reps Mins
	<b>Friday</b>	Reps Mins	Reps Mins	Reps Mins
	<b>Saturday</b>	Reps Mins	Reps Mins	Reps Mins
	<b>Sunday</b>	Reps Mins	Reps Mins	Reps Mins
Please enter the number of repetitions of Effortful swallow you completed in the appropriate time box, and how long it took you to complete.				
<b>COMMENTS</b>				

Please contact Phoebe Macrae on 3786 095 or 027 210 6280 if you have any questions or concerns

**33 x HARD SWALLOWS 3 TIMES PER DAY. TAKE 2 DAYS OFF PER WEEK.**



## Appendix IV: Exercise record sheet – Modified head-lift group

I.D.		Modified head-lift Manoeuvre log sheet		
		TIME OF DAY		
		Morning	Afternoon	Evening
<b>DAYS</b>	<b>Monday</b>	Reps Mins	Reps Mins	Reps Mins
	<b>Tuesday</b>	Reps Mins	Reps Mins	Reps Mins
	<b>Wednesday</b>	Reps Mins	Reps Mins	Reps Mins
	<b>Thursday</b>	Reps Mins	Reps Mins	Reps Mins
	<b>Friday</b>	Reps Mins	Reps Mins	Reps Mins
	<b>Saturday</b>	Reps Mins	Reps Mins	Reps Mins
	<b>Sunday</b>	Reps Mins	Reps Mins	Reps Mins
Please enter the number of repetitions of Head-lift you completed in the appropriate time box, and how long it took to complete.				
<b>COMMENTS</b>				

Please contact Phoebe Macrae on 3786 095 or 027 210 6280 if you have any questions or concerns

**30 X RAPID HEAD-LIFTS (visualize toes and back down) + 3 SUSTAINED HEAD-LIFTS FOR 30sec.**

**COMPLETE 3 TIMES PER DAY. TAKE 2 DAYS OFF EVERY WEEK.**



## Appendix V: Results of alternative analysis – GLM RM-ANOVA

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### AV.1 Corticobulbar excitability results

#### AV.1.1 Submental MEPs recorded during volitional contraction

To investigate if there was a significant difference between one exercise session of effortful swallowing and one exercise session of modified head-lift manoeuvre on area of submental MEPs during volitional contraction, a mixed RM-ANOVA was completed with a between-subject factor of treatment, and a within-subject factor of time. There was no significant effect of treatment, indicating that area of contraction MEPs for each of the two groups did not differ from each other ( $F(1, 32) = .75, p = .39, \eta_p^2 = .02$ ). Additionally, there was no effect of time ( $F(4, 128) = .37, p = 0.83, \eta_p^2 = .01$ ), or time\*treatment ( $F(4, 128) = .95, p = 0.44, \eta_p^2 = .03$ ) on area of MEPs recorded during volitional contraction.

To investigate if there was a significant difference between one exercise session of effortful swallowing and one exercise session of modified head-lift manoeuvre on onset latency of submental MEPs during volitional contraction, a mixed RM-ANOVA was completed with a between-subject factor of treatment, and a within-subject factor of time. There was no significant effect of treatment, indicating that onset latencies of contraction MEPs for each of the two groups did not differ from each other ( $F(1, 32) = .67, p = .42, \eta_p^2 = .02$ ). Additionally, there was no effect of time ( $F(4, 128) = .67, p = 0.61, \eta_p^2 = .02$ ), or time\*treatment ( $F(4, 128) = .20, p = 0.94, \eta_p^2 = .01$ ) on onset latencies of MEPs recorded during volitional contraction.

To check if there was a significant difference between six weeks of effortful swallowing and six weeks of modified head-lift manoeuvre on area of submental MEPs recorded during volitional contraction, a mixed RM-ANOVA was completed with a between-subject factor of treatment, and a within-subject factor of time. There was no significant effect of treatment, indicating that area of contraction MEPs for each of the two groups did not differ from each other ( $F(1, 32) = 3.36, p = .08, \eta_p^2 = .10$ ). Additionally, there was no effect of time ( $F(1, 32) = .28, p = 0.60, \eta_p^2 = .01$ ), or time\*treatment ( $F(1, 32) = 2.23, p = 0.15, \eta_p^2 = .07$ ) on area of MEPs recorded during volitional contraction.

To investigate if there was a significant difference between six weeks of effortful swallowing and six weeks of modified head-lift manoeuvre on onset latencies of submental MEPs recorded during volitional contraction, a mixed RM-ANOVA was completed with a between-subject factor of treatment, and a within-subject factor of time. There was no significant effect of treatment, indicating that onset latencies of contraction MEPs for each of the two groups did not differ from each other ( $F(1, 32) = 3.64, p = .07, \eta_p^2 = .10$ ). Additionally, there was no effect of time ( $F(1, 32) = 5.76, p = 0.02, \eta_p^2 = .15$ ), or time\*treatment ( $F(1, 32) = .72, p = 0.40, \eta_p^2 = .02$ ) on onset latency of MEPs recorded during volitional contraction.

### **AV.1.2 Submental MEPs recorded during volitional swallowing**

To investigate if there was a significant difference between one exercise session of effortful swallowing and one exercise session of modified head-lift manoeuvre on area of submental MEPs during volitional swallowing, a mixed RM-ANOVA was completed with a between-subject factor of treatment, and a within-subject factor of time. There was no significant effect of treatment, indicating that area of swallowing MEPs for each of the two groups did not differ from each other ( $F(1, 29) = .02, p = .90, \eta_p^2 = .00$ ). Additionally, there was no effect of time ( $F(4, 116) = .12, p = 0.98, \eta_p^2 = .00$ ), or time\*treatment ( $F(4, 116) = .52, p = 0.72, \eta_p^2 = .02$ ) on area of MEPs recorded during volitional swallowing.

To investigate if there was a significant difference between one exercise session of effortful swallowing and one exercise session of modified head-lift manoeuvre on onset latency of submental MEPs during volitional swallowing, a mixed RM-ANOVA was completed with a between-subject factor of treatment, and a within-subject factor of time. There was no significant effect of treatment, indicating that onset latencies of swallowing MEPs for each of the two groups did not differ from each other ( $F(1, 29) = .00, p = 1.00, \eta_p^2 = .00$ ). Additionally, there was no effect of time ( $F(4, 116) = .12, p = 0.98, \eta_p^2 = .00$ ), or time\*treatment ( $F(4, 116) = .62, p = 0.65, \eta_p^2 = .02$ ) on onset latencies of MEPs recorded during volitional swallowing.

To check if there was a significant difference between six weeks of effortful swallowing and six weeks of modified head-lift manoeuvre on area of submental MEPs recorded during volitional swallowing, a mixed RM-ANOVA was completed with a between-subject factor of treatment, and a within-subject factor of time. There was no significant effect of treatment, indicating that area of swallowing MEPs for each of the two groups did not differ from each other ( $F(2, 28) = .40, p = .68, \eta_p^2 = .03$ ). Additionally, there was no effect of time ( $F(1, 28) =$

.44,  $p = 0.51$ ,  $\eta_p^2 = .02$ ), or time\*treatment ( $F(2, 28) = .79$ ,  $p = 0.47$ ,  $\eta_p^2 = .05$ ) on area of MEPs recorded during volitional swallowing.

To investigate if there was a significant difference between six weeks of effortful swallowing and six weeks of modified head-lift manoeuvre on onset latencies of submental MEPs recorded during volitional swallowing, a mixed RM-ANOVA was completed with a between-subject factor of treatment, and a within-subject factor of time. There was no significant effect of treatment, indicating that onset latencies of swallowing MEPs for each of the two groups did not differ from each other ( $F(2, 28) = .70$ ,  $p = .51$ ,  $\eta_p^2 = .05$ ). Additionally, there was no effect of time ( $F(1, 28) = .05$ ,  $p = 0.83$ ,  $\eta_p^2 = .00$ ), or time\*treatment ( $F(2, 28) = 1.50$ ,  $p = 0.24$ ,  $\eta_p^2 = .10$ ) on onset latency of MEPs recorded during volitional swallowing.

## **AV.2 Pharyngeal pressure results**

### **AV.2.1 Upper- and hypo-pharyngeal amplitudes**

To assess if there were significant differences between effortful swallowing and modified head-lift manoeuvre on amplitudes of upper-pharyngeal and hypo-pharyngeal pressures recorded during dry, effortful, and 10 mL water swallows, a mixed RM-ANOVA was completed with treatment as the between-subject factor, and time, swallow type, and sensor as the within-subject factors. There was no significant effect of treatment, indicating that upper-pharyngeal and hypo-pharyngeal pressures for each of the two groups did not differ from each other ( $F(1, 34) = .67$ ,  $p = .42$ ,  $\eta_p^2 = .02$ ). Additionally, there was no effect of time ( $F(1, 34) = 2.70$ ,  $p = 0.11$ ,  $\eta_p^2 = .07$ ), time\*treatment ( $F(1, 34) = .16$ ,  $p = 0.69$ ,  $\eta_p^2 = .01$ ), time\*swallow type\*treatment ( $F(2, 68) = .13$ ,  $p = 0.88$ ,  $\eta_p^2 = .00$ ), time\*sensor\*treatment ( $F(1, 34) = .42$ ,  $p = 0.52$ ,  $\eta_p^2 = .01$ ), or time\*swallow type\*sensor\* treatment ( $F(2, 68) = .33$ ,  $p = 0.72$ ,  $\eta_p^2 = .01$ ) on amplitude of upper- and hypo-pharyngeal pressures.

### **AV.2.2 UES amplitudes**

To check for significant differences between effortful swallowing and modified head-lift manoeuvre on magnitude of UES pressures recorded during dry, effortful, and 10 mL water swallows, a mixed RM-ANOVA was completed with treatment as the between-subject factor, and time and swallow type as the within-subject factors. There was no significant effect of treatment, indicating that UES pressures for each of the two groups did not differ from each other ( $F(1, 34) = .01$ ,  $p = .93$ ,  $\eta_p^2 = .00$ ). Additionally, there was no effect of time ( $F(1, 34) =$

.07,  $p = 0.80$ ,  $\eta_p^2 = .00$ ), time\*treatment ( $F(1, 34) = .00$ ,  $p = 0.95$ ,  $\eta_p^2 = .00$ ), or time\*swallow type\*treatment ( $F(2, 68) = .31$ ,  $p = 0.74$ ,  $\eta_p^2 = .01$ ) on magnitude of UES pressures.

### **AV.2.3 Durations of pharyngeal pressure generation**

To investigate if there were significant differences between effortful swallowing and modified head-lift manoeuvre on durations of pressure generation in the upper-pharynx, hypo-pharynx, UES, on duration between peak of upper-pharyngeal pressure to peak of hypo-pharyngeal pressure, and total swallowing durations recorded during dry, effortful, and 10 mL water swallows, a mixed RM-ANOVA was completed with a between-subject factor of treatment, and within-subject factors of time, swallow type, and duration. There was no significant effect of treatment, indicating that durations of pressure generations for each of the two groups did not differ from each other ( $F(1, 34) = .54$ ,  $p = .47$ ,  $\eta_p^2 = .02$ ). Additionally, there was no effect of time ( $F(1, 34) = .89$ ,  $p = 0.35$ ,  $\eta_p^2 = .03$ ), time\*treatment ( $F(1, 34) = .00$ ,  $p = 0.99$ ,  $\eta_p^2 = .00$ ), time\*swallow type\*treatment ( $F(2, 68) = .14$ ,  $p = 0.87$ ,  $\eta_p^2 = .00$ ), time\*duration\*treatment ( $F(4, 136) = .31$ ,  $p = 0.87$ ,  $\eta_p^2 = .01$ ), or time\*swallow type\*duration\* treatment ( $F(8, 272) = .41$ ,  $p = 0.92$ ,  $\eta_p^2 = .01$ ) on durations of pharyngeal pressures generation.

## **AV.3 Muscle hypertrophy results**

### **AV.3.1 CSA of the anterior belly of the digastric muscle**

To investigate if there was a significant difference between effortful swallowing and modified head-lift manoeuvre on the CSA of the left and right bellies of the anterior belly of digastric muscle, a mixed RM-ANOVA was completed with a between-subject factor of treatment, and within-subject factors of time and muscle belly. There was no significant effect of treatment, indicating that CSA measures of the anterior belly of the digastric muscle for each of the two groups did not differ from each other ( $F(1, 37) = 1.23$ ,  $p = .28$ ,  $\eta_p^2 = .03$ ). Additionally, there was no effect of time ( $F(1, 37) = 1.13$ ,  $p = 0.29$ ,  $\eta_p^2 = .03$ ), time\*treatment ( $F(1, 37) = .16$ ,  $p = 0.69$ ,  $\eta_p^2 = .00$ ), or time\*muscle belly\*treatment ( $F(1, 37) = 5.67$ ,  $p = 0.02$ ,  $\eta_p^2 = .13$ ) on CSA of the anterior belly of digastric muscle.

### **AV.3.2 CSA of the geniohyoid muscle**

To investigate if there was a significant difference between effortful swallowing and modified head-lift manoeuvre on the CSA of the geniohyoid muscle, a mixed RM-ANOVA was completed with a between-subject factor of treatment, and a within-subject factor of time.



There was no significant effect of treatment, indicating that CSA measures of the geniohyoid muscle for each of the two groups did not differ from each other ( $F(1, 37) = .00, p = .96, \eta_p^2 = .00$ ). Additionally, there was no effect of time ( $F(1, 37) = 7.53, p = 0.01, \eta_p^2 = .17$ ), or time\*treatment ( $F(1, 37) = .00, p = 0.96, \eta_p^2 = .00$ ) on CSA of the geniohyoid muscle.

## **AV.4 Hyoid displacement results**

To investigate if there was a significant difference between effortful swallowing and modified head-lift manoeuvre on the magnitude of hyoid displacement during swallowing, a mixed RM-ANOVA was completed with a between-subject factor of treatment, and a within-subject factor of time. There was no significant effect of treatment, indicating that measures of hyoid displacement for each of the two groups did not differ from each other ( $F(1, 37) = .00, p = 1.00, \eta_p^2 = .00$ ). Additionally, there was no effect of time ( $F(1, 37) = .00, p = 0.97, \eta_p^2 = .00$ ), or time\*treatment ( $F(1, 37) = .03, p = 0.87, \eta_p^2 = .00$ ) on hyoid displacement during swallowing.

## **AV.5 Submental muscle activation results**

### **AV.5.1 Muscle activation during volitional contraction**

To investigate if there was a significant difference between effortful swallowing and modified head-lift manoeuvre on the amplitude of muscle activation during volitional contraction of the submental muscles, a mixed RM-ANOVA was completed with a between-subject factor of treatment, and a within-subject factor of time. There was no significant effect of treatment, indicating that measures of muscle activation during volitional contraction for each of the two groups did not differ from each other ( $F(1, 29) = .26, p = .62, \eta_p^2 = .01$ ). Additionally, there was no effect of time ( $F(1, 29) = .02, p = 0.88, \eta_p^2 = .00$ ), or time\*treatment ( $F(1, 29) = .19, p = 0.67, \eta_p^2 = .01$ ) on submental muscle activation during volitional contraction.

### **AV.5.2 Muscle activation during volitional swallowing**

To investigate if there was a significant difference between effortful swallowing and modified head-lift manoeuvre on the amplitude of submental muscle activation during volitional swallowing, a mixed RM-ANOVA was completed with a between-subject factor of treatment, and a within-subject factor of time. There was no significant effect of treatment, indicating that measures of muscle activation during volitional swallowing for each of the two groups did not differ from each other ( $F(1, 29) = 2.80, p = .11, \eta_p^2 = .10$ ). There was no effect of time

( $F(1, 29) = .13, p = 0.72, \eta_p^2 = .01$ ), or time\*treatment ( $F(1, 29) = .05, p = 0.83, \eta_p^2 = .00$ ) on submental muscle activation during volitional swallowing.

## **AV.6      Summary**

With the Bonferroni adjusted  $p$ -value of 0.0004 required for significance at the 0.05 level, there are no significant effects of treatments on any of the measures revealed using mixed RM-ANOVA. As these results do not differ to those reported in Chapter 13 of the thesis, further discussion regarding the lack of significant findings are discussed in Chapter 14, and do not warrant further discussion here. As mentioned previously, statistical significance is difficult to achieve with a large number of comparisons, especially when an overly conservative estimate of adjustment is employed, such as the Bonferroni method. Therefore, the provision of estimated effects and their 95% confidence intervals is provided in Chapter 13, and interpretation of these in Chapter 14.

Appendix VI: Raw data plots

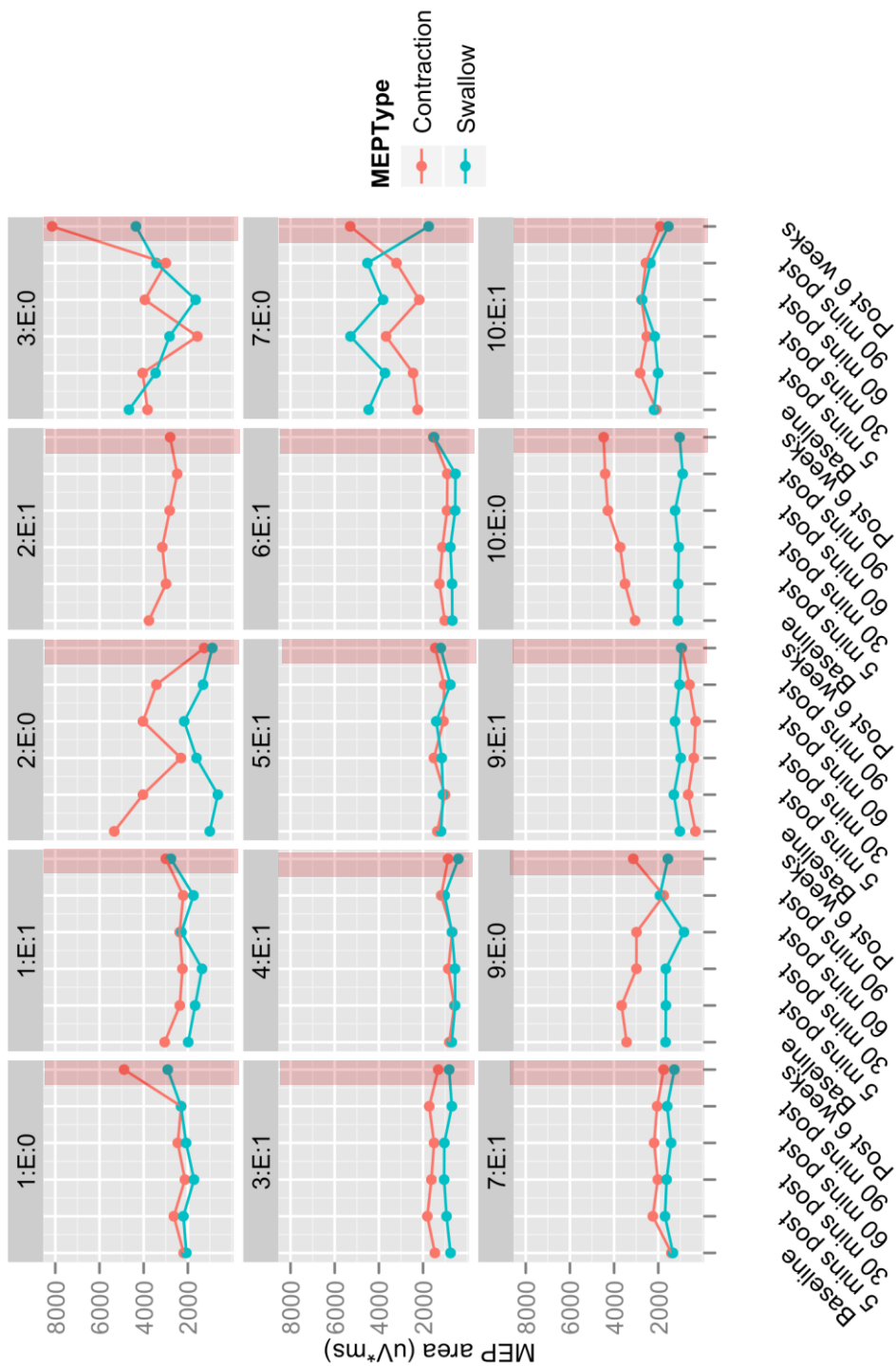


Figure AVI.1. Raw data for MEP area for participants assigned to the effortful-swallowing group. The 6 points on the x-axis represent the 6 time points at which MEPs were recorded. Note the outcome session completed 6-weeks following exercise initiation is highlighted in red to distinguish the difference between those recorded on the same day (baseline, 5 min post, 30 min post, 60 min post and 90 min post) and the outcome session recorded on a separate day (post 6 weeks).

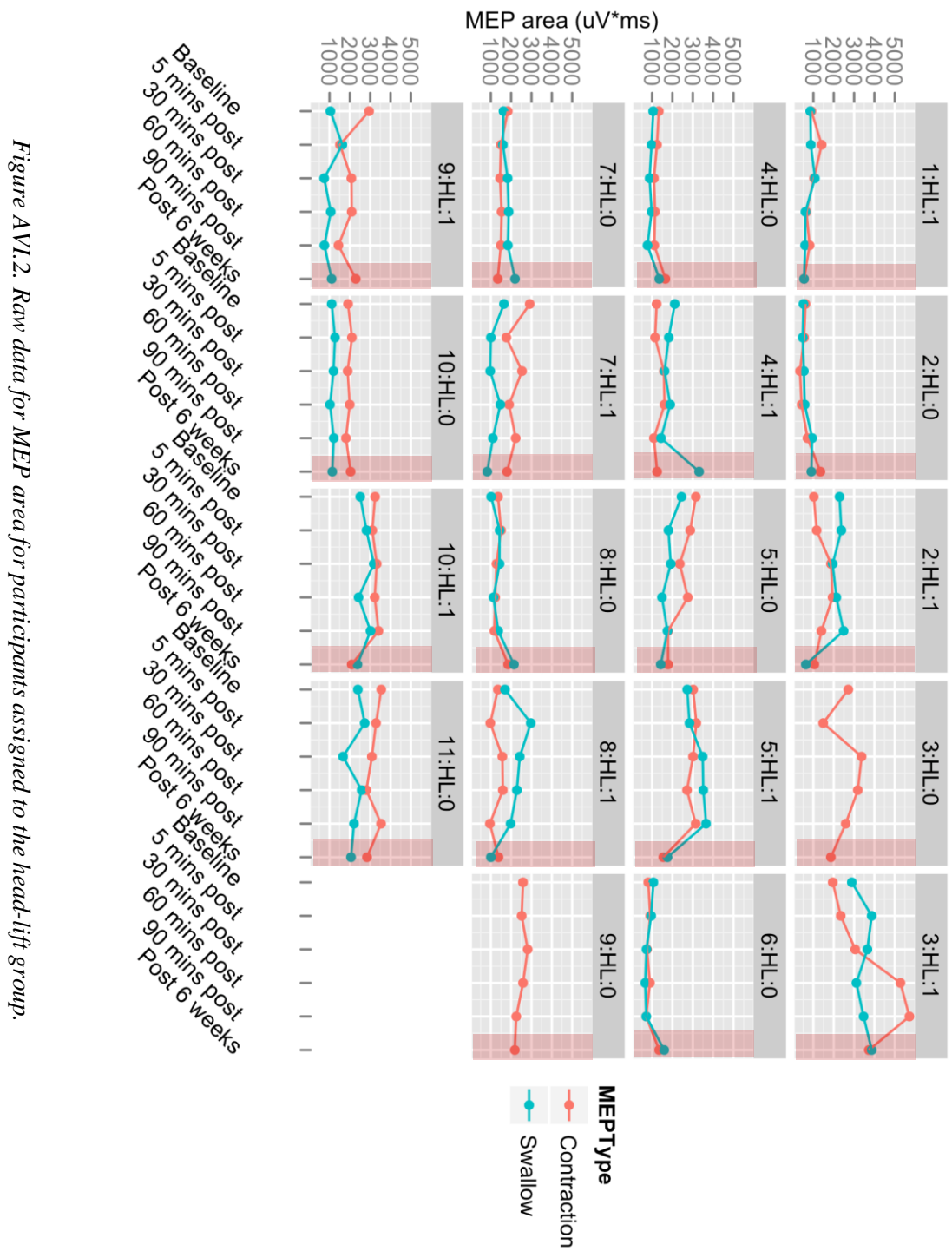


Figure AVI.2. Raw data for MEP area for participants assigned to the head-lift group.



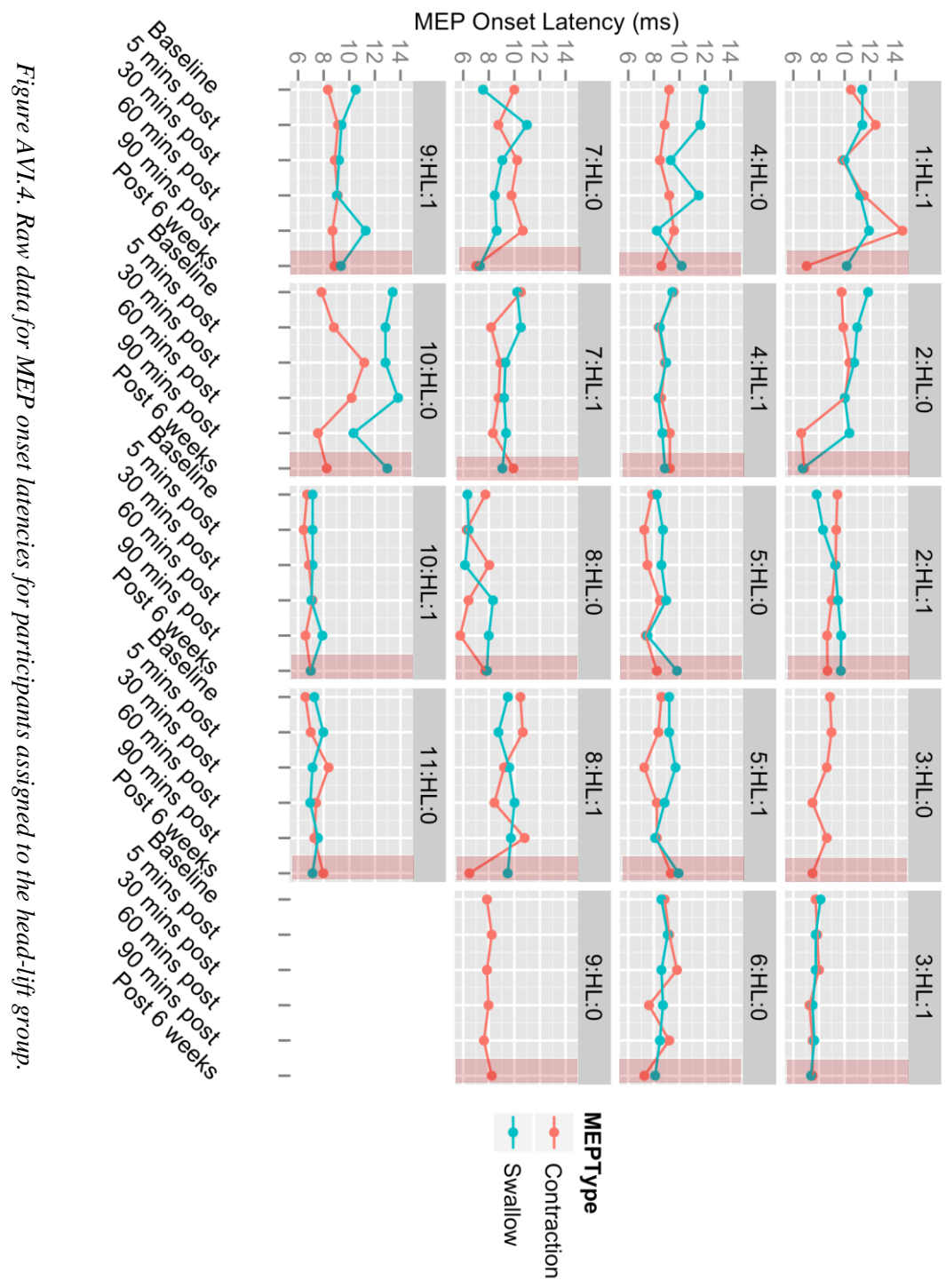


Figure AVI.4. Raw data for MEP onset latencies for participants assigned to the head-lift group.

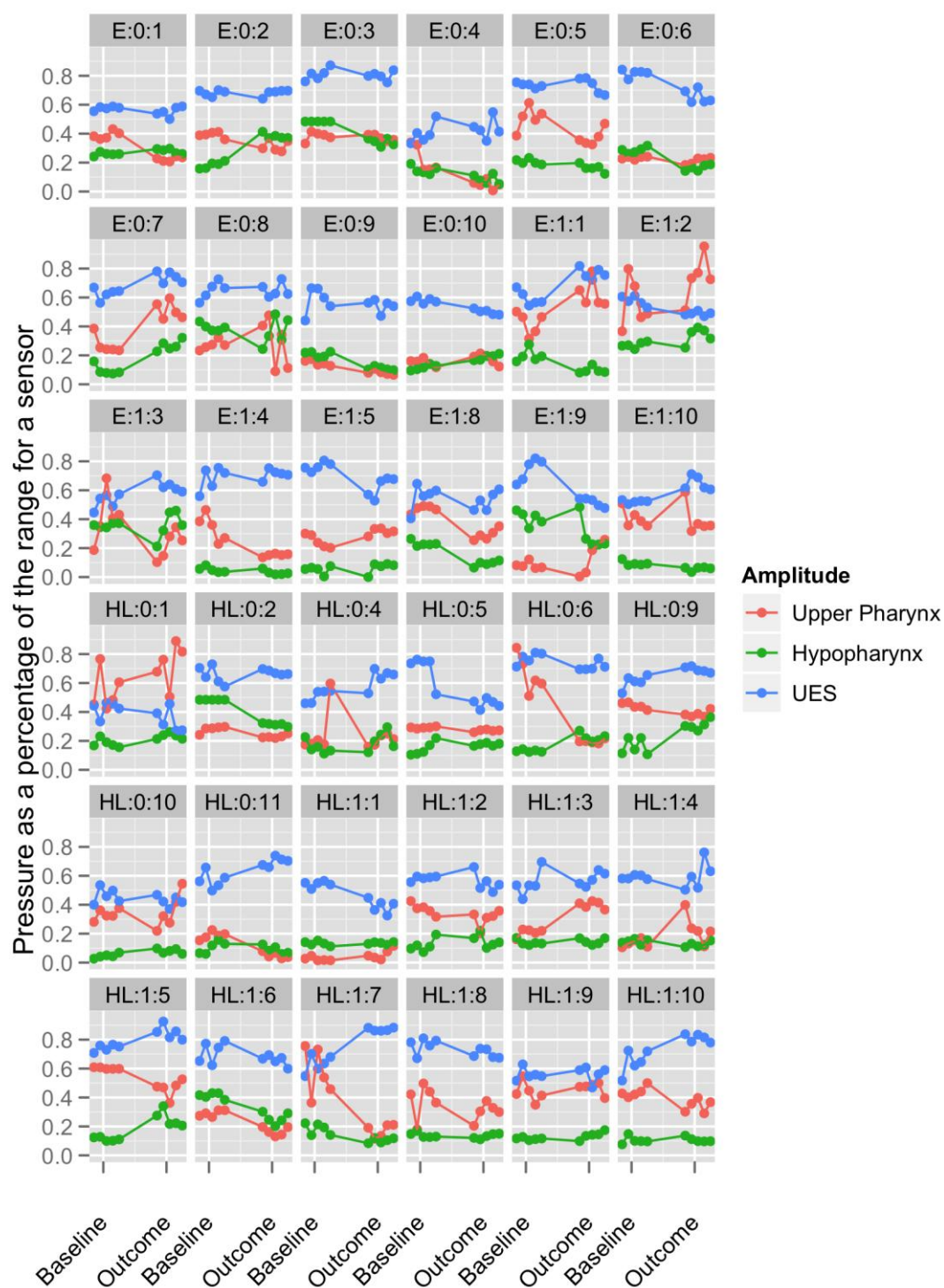


Figure AVI.5. Raw data for pharyngeal pressure amplitudes during dry swallows for both the effortful-swallowing and modified head-lift groups. The five points at each session represent the five trials.



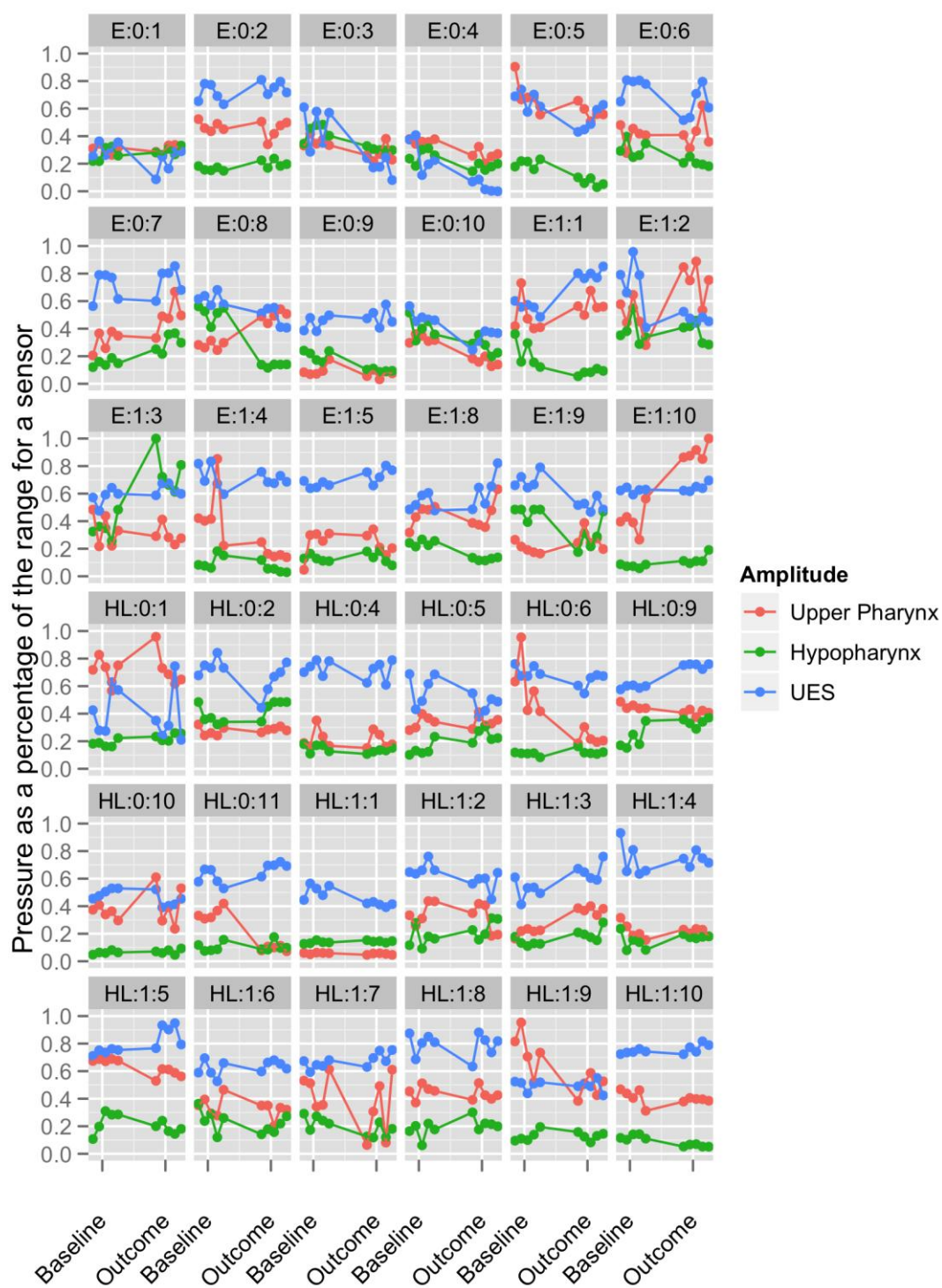


Figure AVI.6. Raw data for pharyngeal pressure amplitudes during effortful swallows for both the effortful-swallowing and modified head-lift groups.



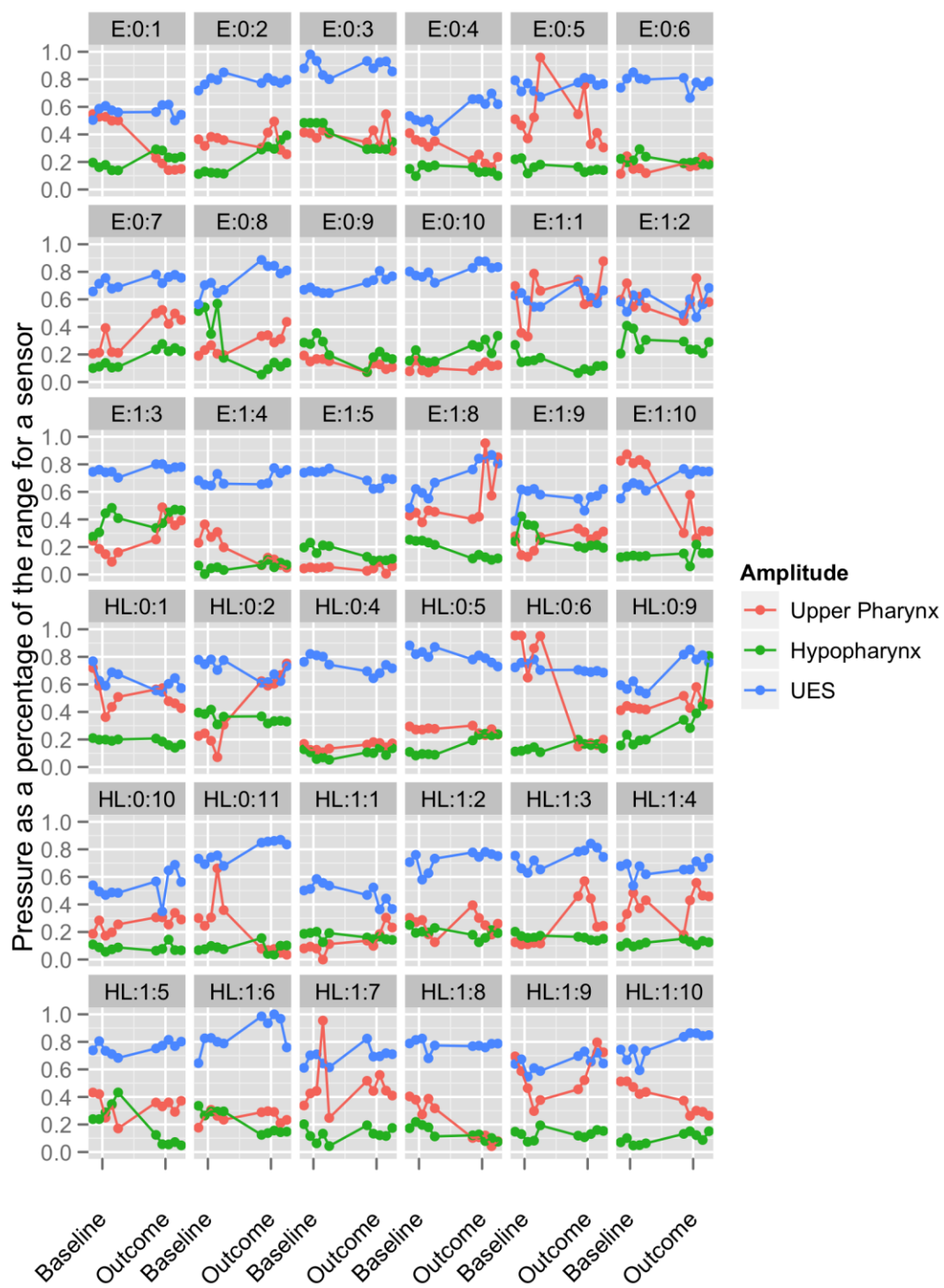


Figure AVI.7. Raw data for pharyngeal pressure amplitudes during 10 mL water swallows for both the effortful-swallowing and modified head-lift groups.

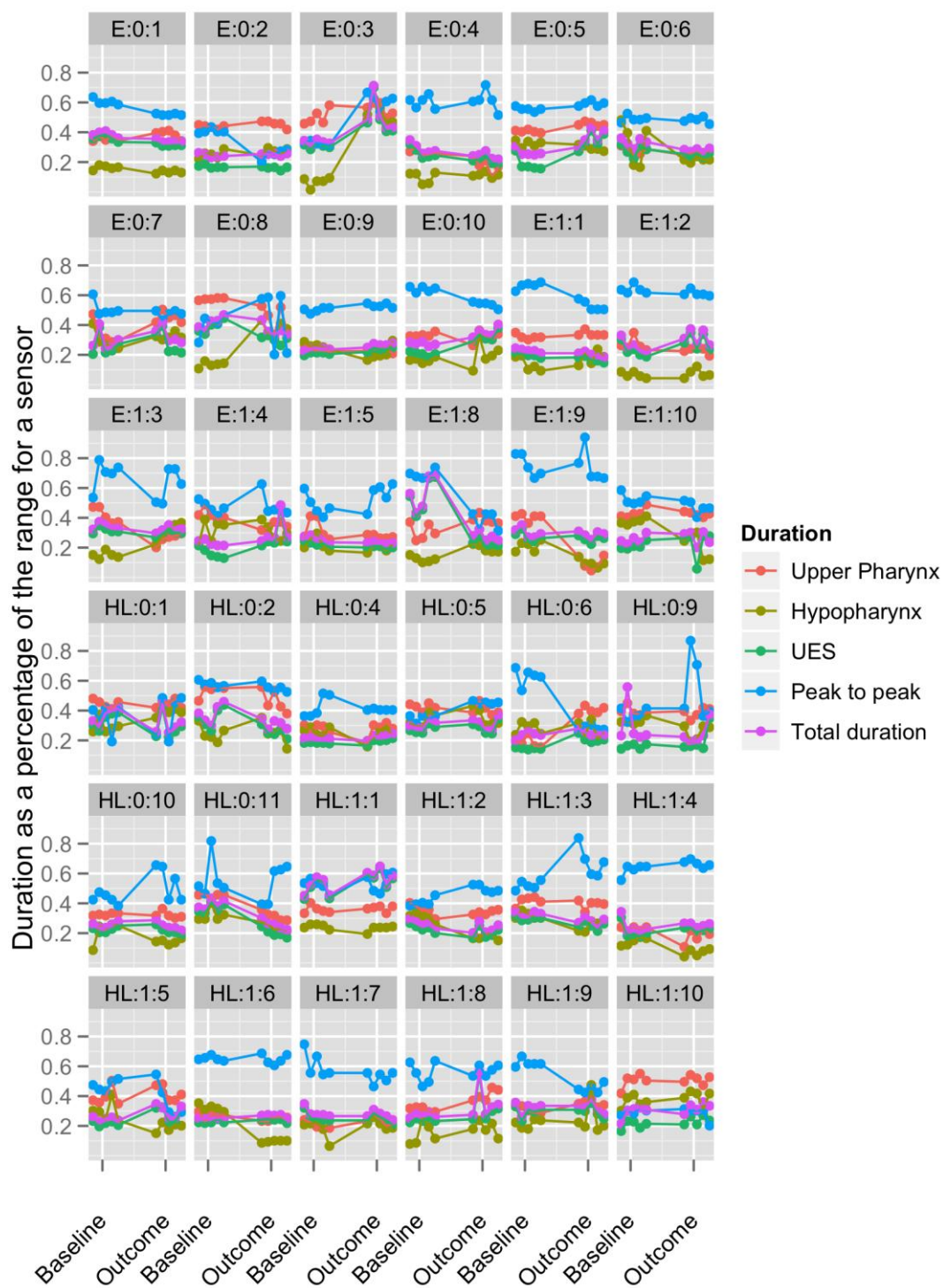


Figure AVI.8. Raw data for duration of pharyngeal pressure generation during dry swallows for both the effortful-swallowing and modified head-lift groups.

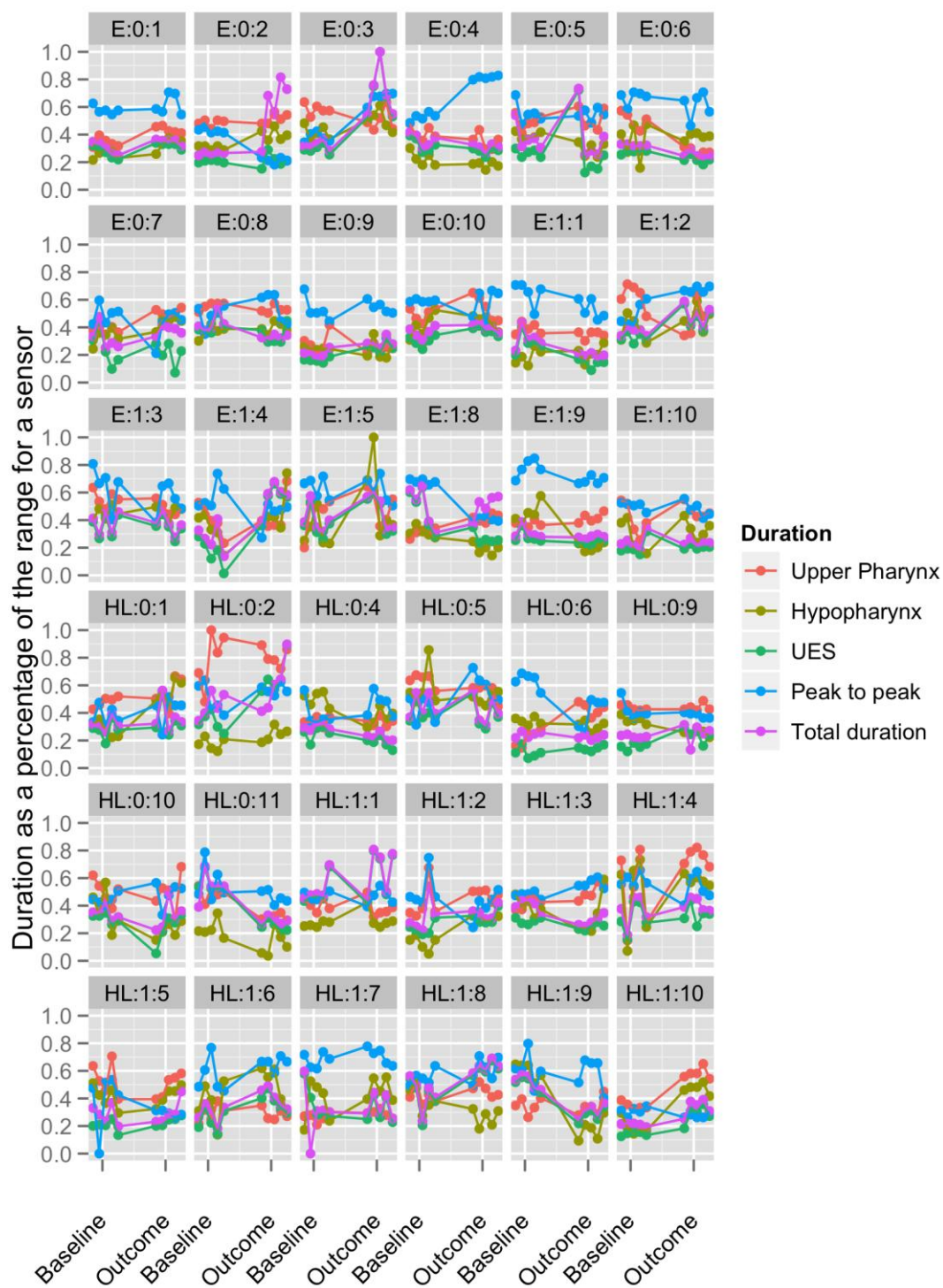


Figure AVI.9. Raw data for duration of pharyngeal pressure generation during effortful swallows for both the effortful-swallowing and modified head-lift groups.



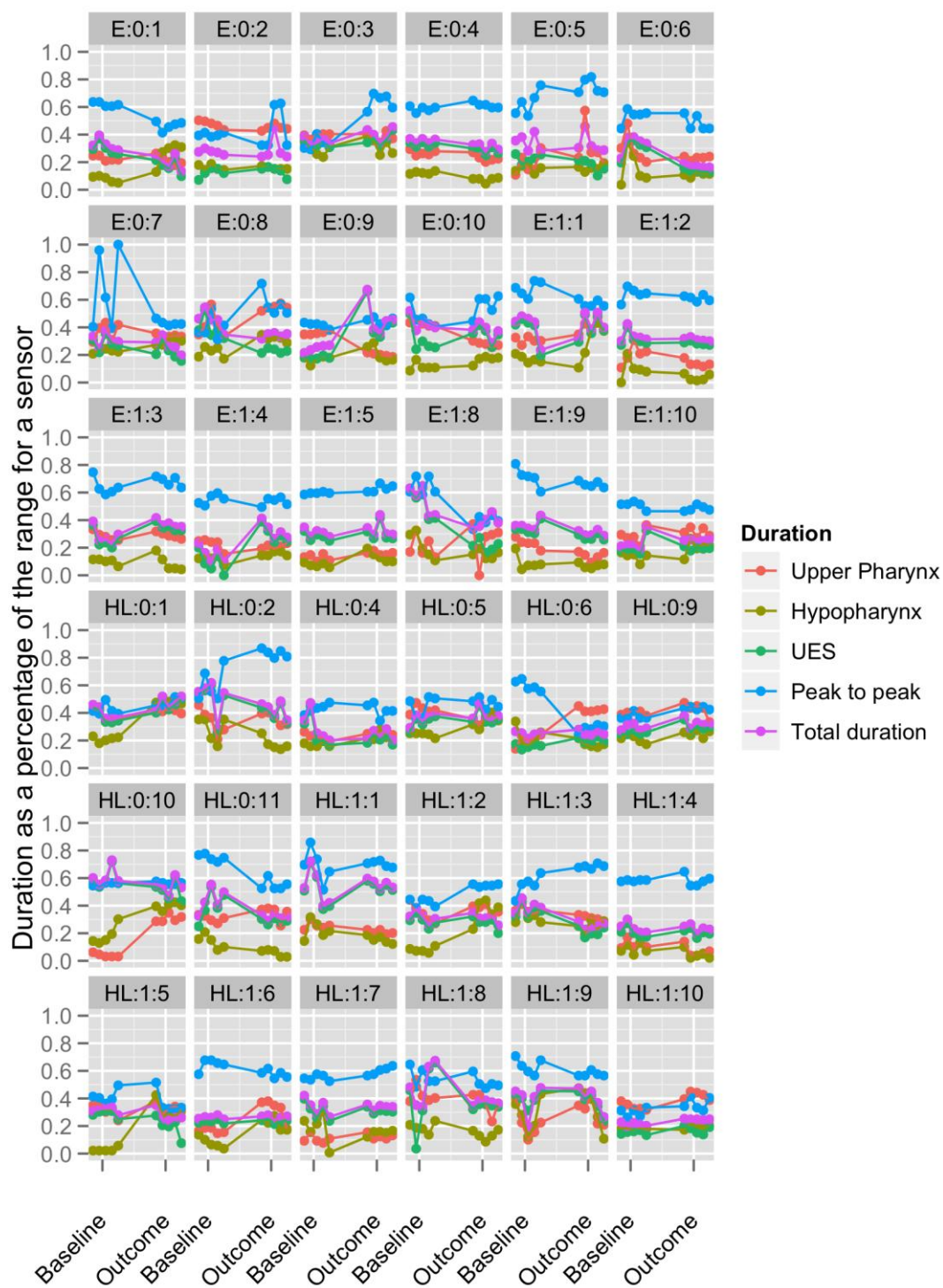


Figure AVI.10. Raw data for duration of pharyngeal pressure generation during 10 mL water swallows for both the effortful-swallowing and modified head-lift groups.

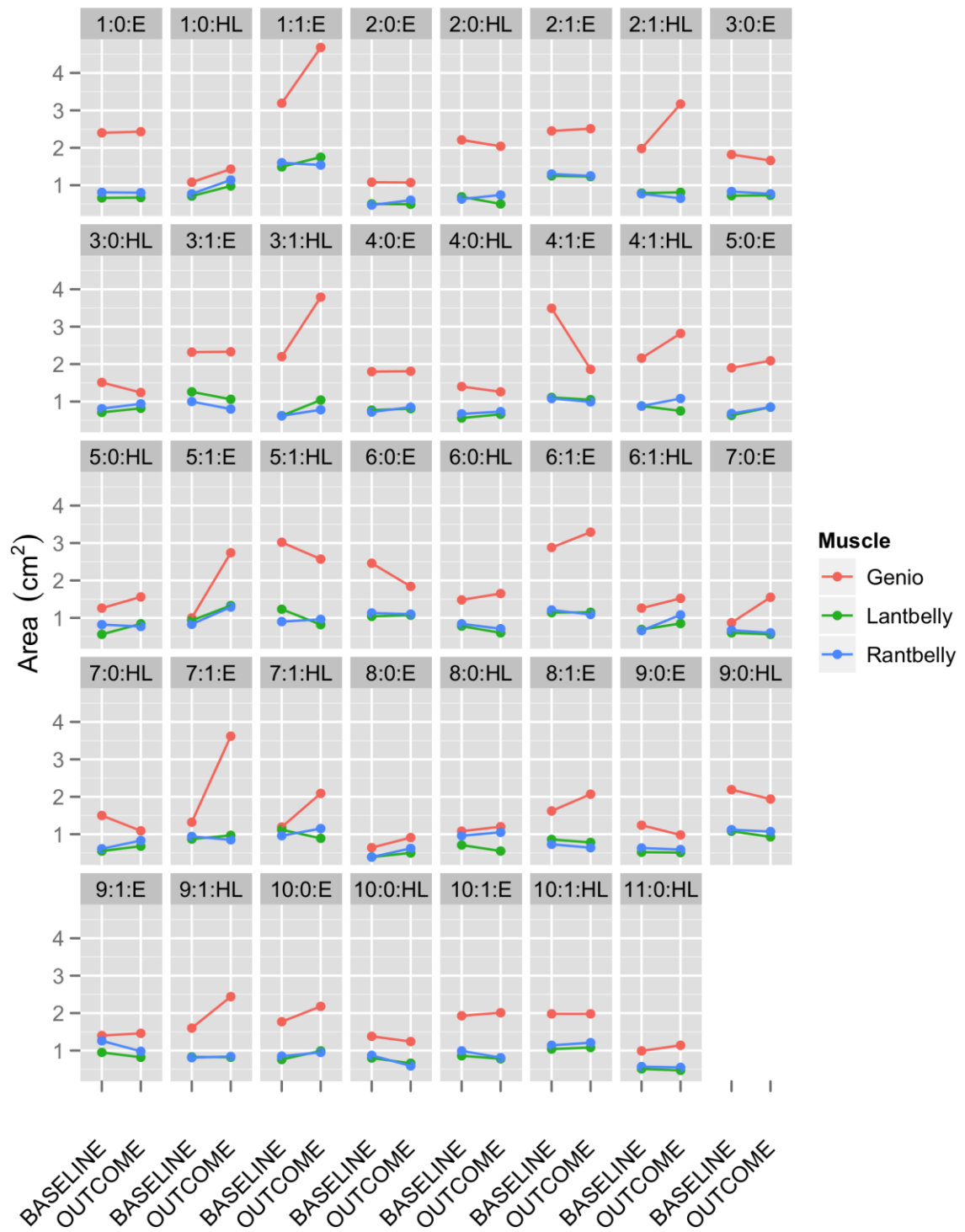


Figure AVI.11 Raw data for CSA of the left (green) and right (blue) anterior belly of digastric muscles and the combined geniohyoid (red) muscles for each participant.

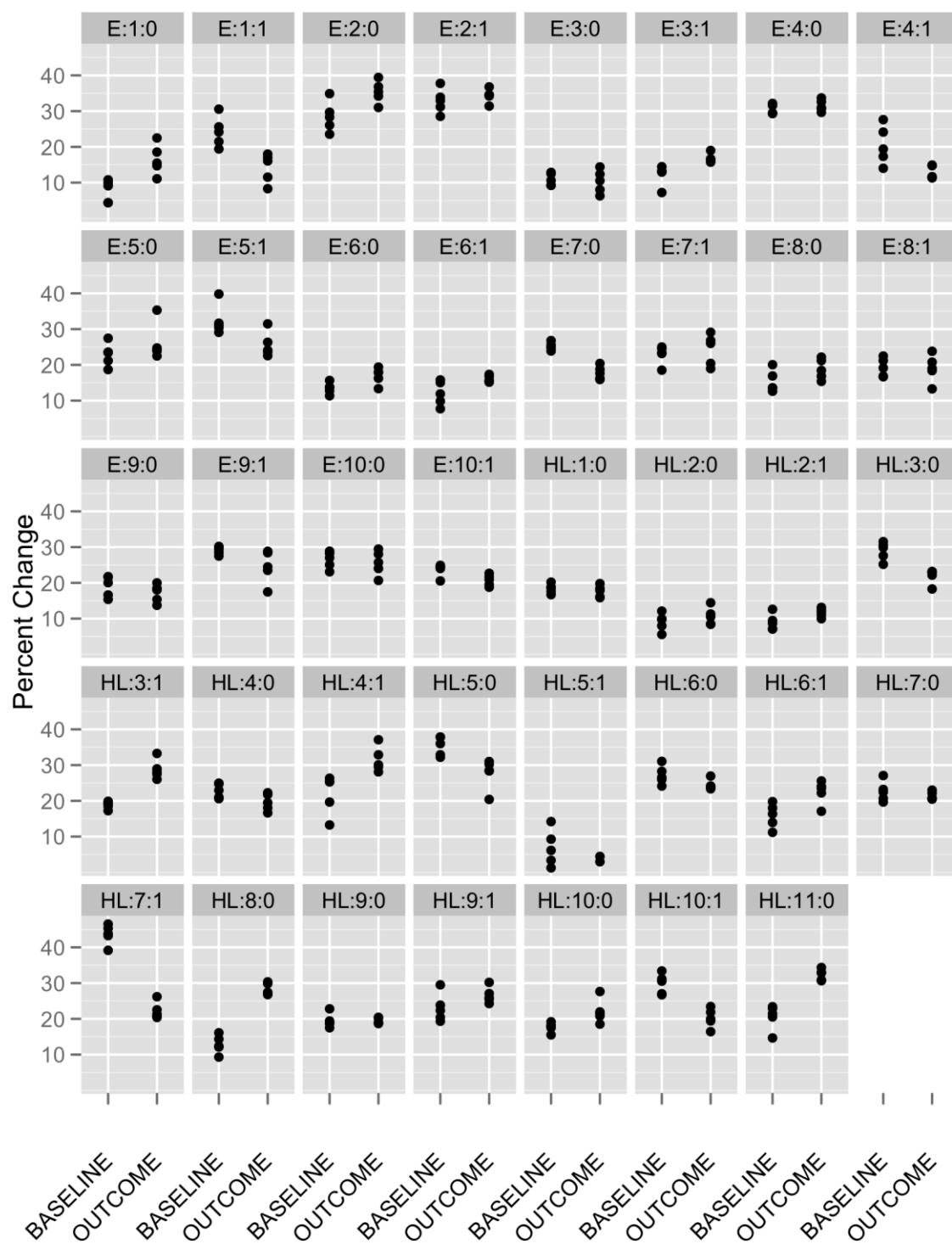


Figure AVI.12. Raw data for percent change of hyoid displacement from rest for each participant. The five points at each time point represent the five trials.

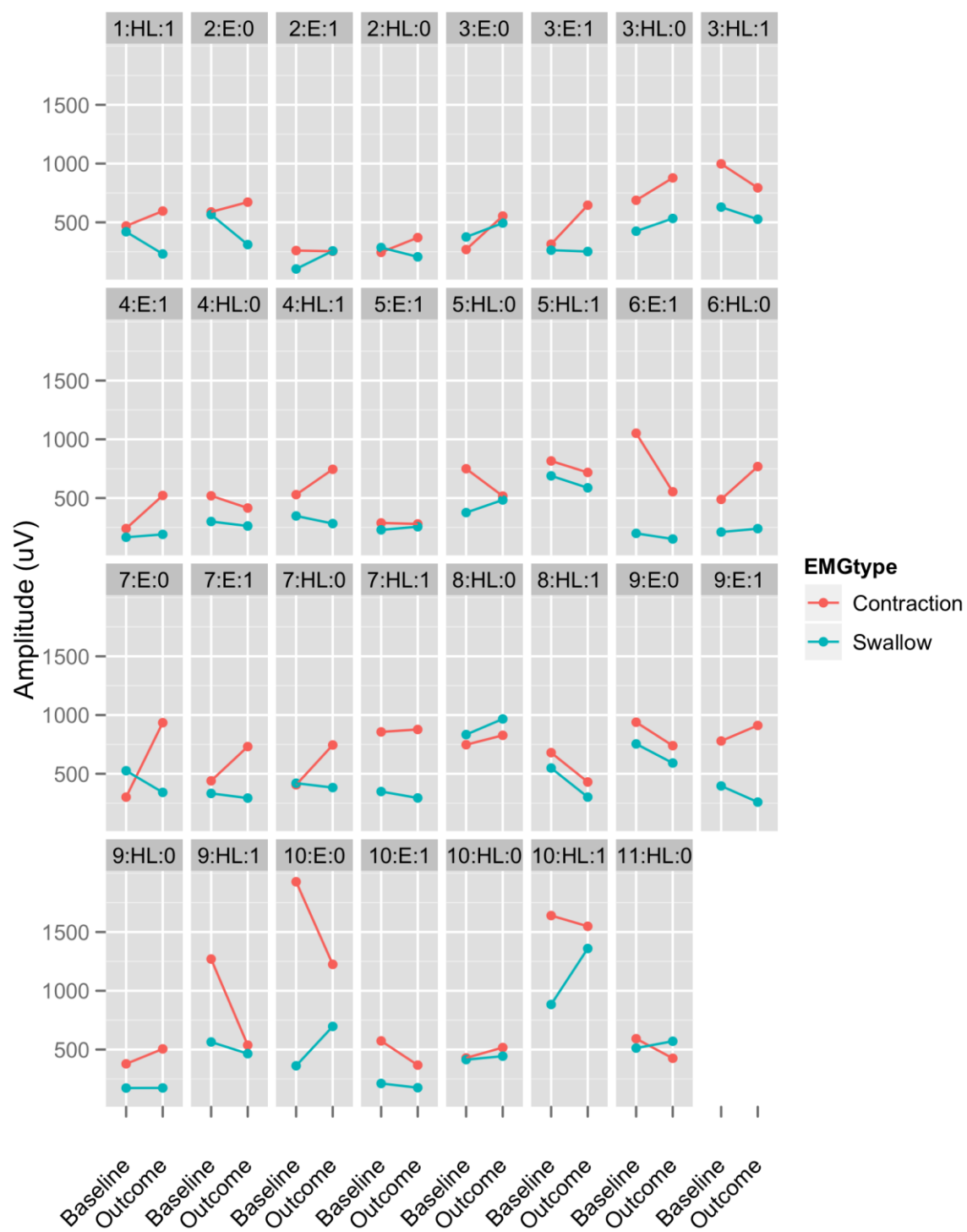


Figure AVI.13. Raw data for sEMG amplitude measures during both maximal voluntary contraction and swallowing for each participant.